ADDENDUM
1936
TO THE
BRITISH PHARMACOPŒIA
1932

PUBLISHED UNDER THE DIRECTION OF

THE GENERAL COUNCIL OF
MEDICAL EDUCATION AND REGISTRATION
OF THE UNITED KINGDOM

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CONTENTS

	PAGE
The General Council of Medical Education and Registration of the United Kingdom	v
Notice	vi
Preface	vii
The British Pharmacopœia Commission	ix
Introduction	xi
Corrigenda in the First Issue of the British Pharmacopœia, 1932 (September, 1932)	xxi
Additions to the British Pharmacopœia, 1932	xxiv
Deletion from the British Pharmacopœia, 1932	xxiv
Monographs of the British Pharmacopœia, 1932, which are amended by the Addendum, 1936	xxiv
General Notices	1
Monographs	3
Appendices	75
Index	119

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NOTICE

By Section 2 of the Medical Council Act, 1862, the exclusive right of publishing, printing, and selling the British Pharmacopœia is vested in the General Council of Medical Education and Registration of the United Kingdom.

The British Pharmacopœia, 1932, superseded previous issues of the British Pharmacopœia, being for all purposes deemed to be substituted for such previous issues.

This Addendum alters and amends the British Pharmacopœia, 1932. The General Notices and Appendices included in the British Pharmacopœia, 1932, apply to all matter contained in this Addendum, unless the contrary is specifically stated.

The Monographs of this Addendum have the same authority as that of the British Pharmacopœia, 1932, to which they are additional, or as that hitherto possessed by Monographs which they now replace. Monographs of the British Pharmacopœia, 1932, which are amended by this Addendum have, as amended, the same authority as that hitherto possessed by the Monographs before emendation.

PREFACE

TO THE ADDENDUM, 1936, TO THE BRITISH PHARMACOPŒIA, 1932

SECTION 54 of the Medical Act, 1858, provides that the General Council of Medical Education and Registration of the United Kingdom 'shall cause to be published under their direction a Book containing a list of medicines and compounds, and the manner of preparing them, together with the true weights and measures by which they are to be prepared and mixed, and containing such other matter and things relating thereto as the General Council shall think fit, to be called "The British Pharmacopœia"; and the General Council shall cause to be altered, amended, and republished, such Pharmacopœia as often as they shall deem it necessary.'

The term of office of the British Pharmacopœia Commission which prepared, under the general direction of the Council, acting through the Pharmacopœia Committee of the Council, the sixth British Pharmacopœia, which was published in 1932, expired on the 30th September, 1933, and the Commission was reconstituted with effect from the 1st October, 1933, as follows:—

A. P. BEDDARD, M.D. (*Chairman*)

R. R. BENNETT, B.Sc.	P. HARTLEY, C.B.E., M.C., D.Sc.
O. L. V. S. DE WESSELOW, D.M.	B. F. HOWARD
J. A. GUNN, M.D.	D. HUNTER, M.D.
	T. TICKLE, B.Sc.

The Sub-Committee on the British Pharmacopœia of the Committee of Civil Research, of which Lord Macmillan was Chairman, recommended, in the paragraphs of their

Report (Cmd. 3101 of 1928) which relate to the period of publication of the Pharmacopœia, that ten years should be regarded as a reasonable interval between successive issues, and that suitable provision should be made during these decennial intervals for supplementing the current issue by the publication of Addenda to the Pharmacopœia.

The present Addendum, 1936, to the British Pharmacopœia, 1932, is the first Addendum to the sixth British Pharmacopœia published in accordance with the recommendations of the Sub-Committee. It has been prepared by the British Pharmacopœia Commission and approved by the Pharmacopœia Committee of the Council in the discharge of the duty entrusted to them by the Standing Orders of the Council to deal with all matters relating to the preparation and publication of the British Pharmacopœia.

The Addendum, 1936, alters and amends the British Pharmacopœia, 1932, by the deletion of one article; by the addition of certain articles and preparations; and by the variation, in the light of knowledge which has since become available, of the monographs relating to other articles and preparations.

The Pharmacopœia Committee of the Council, in a Report made by it to the Council in accordance with the Standing Orders, has conveyed to the Council a cordial expression of its appreciation of the close and sustained labours which have been devoted to the important task of preparing the Addendum, primarily by the Chairman and Members of the British Pharmacopœia Commission, with their Secretary, Mr. C. H. Hampshire, M.B., B.Sc.; and also by the numerous persons and bodies, both in this country and abroad, by whose collaboration that task has been facilitated in the various particulars specified in the Introduction to the Addendum.

General Medical Council Office,
44 Hallam Street, Portland Place,
London, W.1.

THE BRITISH PHARMACOPŒIA COMMISSION 1933–1936

Chairman: A. P. BEDDARD, M.D., Consulting Physician to Guy's Hospital.

R. R. BENNETT, B.Sc., Chairman of the British Pharmaceutical Conference, 1928 and 1929.

O. L. V. S. DE WESSELOW, D.M., Professor of Medicine in the University of London.

J. A. GUNN, M.D., Professor of Pharmacology in the University of Oxford.

P. HARTLEY, C.B.E., M.C., D.Sc., Director of Biological Standards, the National Institute for Medical Research, Hampstead.

B. F. HOWARD, Vice-President of the Institute of Chemistry, 1930–1933.

D. HUNTER, M.D., Physician with charge of Out-Patients to the London Hospital.

T. TICKLE, B.Sc., Public Analyst to the County of Devon.

Secretary: C. H. HAMPSHIRE, M.B., B.Sc.

INTRODUCTION

In the introduction to the British Pharmacopœia, 1932, the suggestion was made that, in order to keep the Pharmacopœia more continuously in alignment with the advances in therapeutics and the ancillary Sciences, it might be found expedient to issue from time to time a supplement to the Pharmacopœia. It is in accordance with this anticipation that the present Addendum to the Pharmacopœia has been prepared.

After the publication of the sixth British Pharmacopœia in September, 1932, the Commission (1928–33) which had prepared that Pharmacopœia, remained in office for a further year in order to collect and consider the comments made upon its work.

In October, 1933, the present Pharmacopœia Commission (1933–36) was appointed and, after consideration of the various possible ways of keeping the Pharmacopœia abreast of the requirements it is intended to meet, decided that this could best be attained by the issue of an Addendum, which would be published as nearly as possible four years after the issue of the British Pharmacopœia, 1932.

The Commission appointed the following Sub-Committees to assist :—

1. Clinical Committee.—O. L. V. S. de Wesselow (Chairman), D. Hunter (Vice-Chairman), T. Anwyl-Davies, L. S. T. Burrell, A. W. Bourne, E. Rock Carling, F. R. Fraser, A. M. H. Gray, C. F. Hadfield, P. H. Manson-Bahr, R. Foster Moore, B. T. Parsons-Smith, J. A. Ryle, J. Forest Smith, E. Sprawson, L. J. Witts.

2. PHARMACOLOGY COMMITTEE.—J. A. Gunn (Chairman), J. H. Burn, A. J. Clark, Sir H. H. Dale, W. J. Dilling, J. W. Trevan.

3. BIOLOGICAL PRODUCTS COMMITTEE.—P. Hartley (Chairman). Sub-Committees :—

A. *Serological and Bacteriological Products.*—V. D. Allison, A. Fleming, R. A. O'Brien, G. F. Petrie, W. D. H. Stevenson.

B. *Sterile Solutions.*—V. D. Allison, F. H. Carr, C. E. Coulthard, H. Davis, N. Evers, R. A. O'Brien.

C. *Accuracy of Biological Assays.*—J. H. Burn, Miss K. H. Coward, J. H. Gaddum, J. O. Irwin, G. F. Petrie, J. W. Trevan.

4. PHARMACY AND PHARMACOGNOSY COMMITTEE.—R. R. Bennett (Chairman). Sub-Committees :—

A. *Crude Drugs.*—H. Deane, F. N. Howes, H. O. Meek, J. Small, T. E. Wallis.

B. *Extracts, Liquid Extracts and Tinctures.*—H. Berry, H. Davis, F. W. Gamble, T. Wilson.

C. *Waters, Infusions, Solutions, Spirits and Syrups.*—A. J. Jones, H. B. Mackie, A. R. Melhuish, A. L. Taylor.

D. *Ointments and Miscellaneous Galenicals.*—H. Brindle, B. A. Bull, E. S. Peck, H. Skinner, J. Smith.

5. GENERAL CHEMISTRY COMMITTEE.—B. F. Howard (Chairman). Sub-Committees :—

A. *Alkaloids and Alkaloidal Salts.*—T. A. Henry, H. King, F. L. Pyman.

B. *Organic Chemicals.*—F. H. Carr, A. J. Ewins, H. A. D. Jowett, H. King, W. H. Linnell, A. D. Powell.

C. *Inorganic Chemicals.*—T. T. Cocking, C. E. Corfield, N. Evers, A. J. Ewins, J. R. Nicholls, A. D. Powell.

6. PHARMACEUTICAL CHEMISTRY COMMITTEE.—T. Tickle (Chairman). Sub-Committees :—

A. *Essential Oils.*—C. T. Bennett, S. W. Bradley, T. T. Cocking, C. E. Sage, W. H. Simmons.

B. *Fixed Oils, Fats, Waxes, Resins and Soaps.*—E. R. Bolton, N. Evers, J. R. Nicholls, W. H. Simmons.

C. *Assay of Crude Drugs and Galenicals.*—T. T. Cocking, N. Evers, W. H. Linnell, A. D. Powell, P. A. W. Self (deceased).

D. *Tables, Weights and Measures.*—J. R. Nicholls, V. Stott, R. J. Trump.

7. VITAMIN COMMITTEE.—D. Hunter (Chairman), A. L. Bacharach, F. H. Carr, Miss H. Chick, Miss K. H. Coward, J. C. Drummond, N. Evers, Miss E. M. Hume, Miss H. M. M. Mackay.

8. EDITORIAL COMMITTEE.—A. P. Beddard (Chairman), J. A. Gunn, D. Hunter.

In preparing this Addendum, the Commission has adhered to the general principles followed in the preparation of the British Pharmacopœia, 1932, which are set forth in the Introduction to that volume.

The Commission has reviewed the drugs which have been introduced, or which have come into increased use, since the publication of the British Pharmacopœia, 1932, and has selected from them, for description in this Addendum, those which have now become of sufficient importance in medical practice to require definition in the Pharmacopœia. But in making this selection the Commission has found it necessary to exclude, on account of proprietary monopolies or restrictions, certain drugs which otherwise might have been included.

The Addendum includes—(1) New monographs, or changes in existing monographs, arranged alphabetically under new titles or under titles already in the Pharma-

copœia, (2) Additions to, or changes in, the appendices of the Pharmacopœia.

One monograph of the Pharmacopœia, Solution of Irradiated Ergosterol, has been deleted, and replaced by one describing a preparation of Calciferol.

Four monographs, those dealing with Acriflavine, Sterilised Water, Physiological Solution of Sodium Chloride and Cod-liver Oil, have been rewritten. In the case of Cod-liver Oil the changes are important; the antimony trichloride test has been deleted, and minimal requirements for vitamins A and D have been introduced.

Three antitoxins and two antibacterial sera are included in the Addendum. In each case the requirements described are in conformity with the Therapeutic Substances Act, 1925, and the Regulations made thereunder.

Three vitamins are described in the Addendum:—Ascorbic Acid, Vitamin B_1 (in the form of an Adsorbate), and Calciferol. For the first two of these biological assays are described. The vitamin D content of Calciferol, of the Solution of Calciferol, and of Cod-liver Oil, is determined by the Biological Assay of Antirachitic Vitamin (Vitamin D) contained in the Appendix XV of the Pharmacopœia, as amended by this Addendum.

In each of these cases the International Standard and Unit are adopted. Certain other substances for which International Standards and Units are provided, however, have not been included. β-Carotene is not described, but its use as the standard for the determination of Vitamin A is adopted.

For the assay of vitamin A in Cod-liver Oil a biological method, and a spectrophotometric method are described. The latter does not measure the presence of vitamin A directly, but merely shows the presence of some substance having a physical property in common with vitamin A.

This method does not guarantee that any or all of the substance estimated is vitamin A. Therefore the biological assay of vitamin A is to be regarded as decisive.

Similarly International Standards and Units for some of the sex hormones are now available. Rapid advances in the production of allied compounds, having greater therapeutic effects, are however taking place and therefore, in view of the fact that the Pharmacopœial standards must remain unchanged for some years, it has not been thought advisable to include these substances.

Since the publication of the British Pharmacopœia, 1932, the supply of the International Standard Digitalis Powder, containing 1 Unit of activity in 0·1 gramme, has been exhausted. There has now been substituted for it a new powder whose strength is such that it contains 1 Unit of activity in 0·08 gramme. The adjustments in the British Pharmacopœia, 1932, necessitated by this change, are made in this Addendum.

The changes in Pharmacopœial monographs are indicated by reference to the pages of the British Pharmacopœia, 1932.

In the course of the work of preparing this Addendum the Pharmacopœia Commission has issued the following reports containing the recommendations made to it by the Sub-Committees :—

No. 9. Collected Reports of Committees on Material Prepared for an Addendum to the British Pharmacopœia, 1932, February, 1936.

No. 10. Report of the Sub-Committee on the Accuracy of Biological Assays, August, 1936.

In Appendix XV of the British Pharmacopœia, 1932, which deals with biological assays, no uniform method of expressing limits of error is followed, and in some instances no limits of error are stated. When the biological methods

to be recognised in this Addendum had been agreed upon, the Commission appointed a Sub-Committee to determine by modern statistical methods the limits of error of each assay and to advise how they should be expressed. The Sub-Committee dealt with the assays of the three vitamins, the three antitoxins and the two antibacterial sera described in the Addendum, together with that of vitamin D included in the British Pharmacopœia, 1932, and amended in the Addendum, but no recommendations relating to the other assays of the British Pharmacopœia, 1932, were made to the Commission.

A discussion of the data from which these limits have been calculated is published in the Sub-Committee's report. The method of expressing the limits of error is explained in the General Notices under the heading " Errors of Biological Assay ". The limits of error, calculated for each method of assay, are placed at the end of the description of the method.

In this Addendum some alterations are made in the sterilisation procedures of the British Pharmacopœia, 1932. The instructions contained in the British Pharmacopœia, 1932, as amended by this Addendum, are a compromise between what is ideal from the point of view of the bacteriologist and what is capable of achievement under all conditions of dispensing.

In connection with the work of the Committees, the following papers describing research work undertaken at the request of the Commission have appeared :—

' The Strophanthin of Strophanthus Emini ' by I. D. Lamb and S. Smith.

' Sterilisation by Dry Heat at 150° with special reference to Oils ' by C. E. Coulthard.

' A Note on the Sterilisation of Oils ' by R. A. O'Brien and H. J. Parish.

'A Note on the Effect of Sterilisation on Solutions of Calcium Chloride' by C. E. Coulthard and G. F. Hall.

'A Note on the Sterilisation of Injectio Bismuthi B.P.' by C. E. Coulthard.

'The Relative Merits of Maceration and Percolation for the Preparation of Tincture of Digitalis' by H. Berry and H. Davis.

'The Preparation and Preservation of Morphine Injections' by H. Davis.

'An Improved Method for the Estimation of the Essential Oil Content of Drugs' by T. T. Cocking and G. Middleton.

From October, 1932, to October, 1933, the work of the Research Assistant to the Pharmacopœia Commission was carried out in the laboratories of the Pharmaceutical Society of Great Britain and the following papers were published :—

'The Keeping Properties of Liquor Arsenicalis' by E. M. Smelt.

'The Keeping Properties of Liquid Extract of Ergot' by E. M. Smelt.

'Chemical Tests for Strophanthus' by E. M. Smelt.

The Commission desires to record its thanks to the Pharmaceutical Society for providing the necessary accommodation for these researches.

In November, 1933, a laboratory for research on Pharmacopœial problems was instituted in the building of the General Medical Council, and the following papers from it have been published :—

'A Note on the Sulphuric Acid Test for Liquid Paraffin' by C. H. Hampshire and G. R. Page.

'Notes on Some Pharmacopœial Tests—I. Quinine Ethyl Carbonate; Atropine Sulphate; Potash Alum; Aloin; Solution of Cresol with Soap' by G. R. Page.

'The Determination of Camphor in Galenicals by means of 2 : 4-Dinitrophenylhydrazine' by C. H. Hampshire and G. R. Page.

'The Assay of Strong Ointment of Mercuric Nitrate' by C. H. Hampshire and G. R. Page.

'Notes on Some Pharmacopœial Tests—II. Chiniofon; Codeine; Simple Solution of Iodine; Sodium Phosphate' by G. R. Page.

'The Chemical Assay of Ergot' by C. H. Hampshire and G. R. Page.

In selecting additional substances for description in this Addendum the Commission has received valuable assistance from the Clinical Committee and from the following correspondents :—D. Evan Bedford, J. M. H. Campbell, G. Doyne, H. Gardiner-Hill, Lt.-Col. L. W. Harrison, V. E. Lloyd, S. G. MacDonald, C. A. R. Nitch, H. S. Stannus, Sir J. W. Thomson-Walker.

The Commission acknowledges gratefully the help and advice given by the Committees on scientific and technical subjects, in the preparation of this Addendum. In addition, valuable assistance on special points has been rendered by many correspondents, in particular by G. Barr, Miss M. M. O. Barrie, W. J. Beardsley, Mrs. J. St. J. Blake, L. Boardman, R. K. Callow, A. J. Dey, E. C. Dodds, D. B. Dott, the late H. W. Dudley, H. E. Evans, G. J. W. Ferrey, P. Hamill, L. Harding, C. R. Harington, L. J. Harris, W. N. Haworth, E. L. Hirst, C. R. Houseman, J. G. Jackson, C. Jensen, T. J. Johnston, Mrs. K. Lathbury, F. H. Lees, G. Middleton, A. S. Parkes, J. O. Robinson, Miss M.

Llewellyn Smith, S. Smith, S. W. F. Underhill, J. Walmsley, S. S. Zilva.

The Commission has received much valuable assistance from the Australian Committee on Pharmacopœial Revision, from the Canadian Committee on Pharmaceutical Standards, from the Committee in India on Pharmacopœial Revision and from the Department of Public Health for the Union of South Africa. The information and comments received from these sources have been of material assistance in the endeavour to adjust the Addendum to the needs of the Empire.

It is the pleasant duty of the Commission to record the active co-operation over a number of years between the Committee of Revision of the United States Pharmacopœia and the British Pharmacopœia Commission. An interchange of views has taken place on many subjects, but perhaps the most fruitful activity has been an effort to harmonise the titles and standards of the two Pharmacopœias. The Commission hopes that this practice, having been once begun, may be continued with advantage to both books.

The following Government Departments and other bodies have co-operated with the Commission in various ways during the preparation of the Addendum :—The Anæsthetics Committee of the Medical Research Council and the Royal Society of Medicine, the Association of British Chemical Manufacturers, the Board of Customs and Excise, the British Disinfectant Manufacturers' Association, the British Standards Institution, the Department of Health of New Zealand, the Federation of British Industries, the Government Laboratory, the Imperial Institute, the Lister Institute of Preventive Medicine, the London County Council Department of Health, the Medical Research Council, the Ministry of Agriculture and Fisheries, the

National Physical Laboratory, the Pharmaceutical Societies of Great Britain, of Ireland and of Northern Ireland, the Rockefeller Institute for Medical Research, the Royal Botanic Gardens, Kew, and the White Oils Manufacturers Association.

BRITISH PHARMACOPŒIA 1932

CORRIGENDA IN THE FIRST ISSUE (SEPTEMBER 1932)

page	*line*		
xxxi	44	*for* Erythritolis	*read* Erythritylis
xxxvi	25	*for* Rubrum	*read* Rubri
14	11	*for* **Tests**	*read* **Test**
14	11	*for* , dissolved in 200 millilitres of *water*,	*read* of a 0·5 per cent. v/v solution in *water*
16	29	*for* parts	*read* part
51	24	*for* l gramme, boiled with *water* until all the ammonia has been driven off, complies with the *limit test for iron.*	*read* Boil 1 gramme with *water* until all the ammonia has been driven off, and add 5 millilitres of *dilute nitric acid FeT.*; the solution complies with the *limit test for iron.*
52	20	*for* 2·5 grammes, boiled with *water* until all the ammonia has been driven off, complies with the *limit test for iron.*	*read* Boil 2·5 grammes with *water* until all the ammonia has been driven off, and add 5 millilitres of *dilute nitric acid FeT.*; the solution complies with the *limit test for iron.*
54	2	. *after* 90 per cent.	*insert* w/w
57	28	*for* 0·1669	*read* 0·01669
63		*after* line 22	*insert* The number of Units placed in each container must be sufficient to ensure that the number stated on the label is still present at the end of the period during which the preparation is intended to be used.
65	33	*for talc.*	*read talc,*
77	4	*for Synonyms*	*read Synonym*
87	13	*for* determined as	*read* determined on the alcohol-soluble matter from 5 grammes by the method
104	33	*for* 13	*read* 1·3
106	18	*for* 0·02 per cent. w/w	*read* 0·002 per cent. w/v

page	line		
113	24	*after* ***hydroxide***	*insert* , prepared with ***alcohol*** (***95 per cent.***),
131	28	*for* Colchicum Seed	*read* the colchicum seed being assayed
163	14	*after* ***sulphate . . .***'.	*insert* 40 millilitres of the filtrate represents 16 millilitres of the liquid extract of colchicum being assayed.
164	3	*after* below	*insert* , commencing with the words ' wash the residue into a separator . . .'
164	14	*for* Semen	*read* Cormus
164	15	*delete* about	
173	38	*after* per cent.	*insert* v/v
176	33	*after* per cent.	*insert* v/v
179	17	*after* per cent.	*insert* v/v
185	30 & 31	*delete* , as directed under ' Pilula Ferri Carbonatis '	
192	20	*delete dilute*	
192	20	*for* 1	*read* 0·1
192	22	*after* produced	*insert* immediately
211	5	*for* Mercuric Oxide	*read* Yellow Mercuric Oxide
226	6	*for* **2 to 4 mils. 30 to 60 minims.**	*read* **2 to 8 mils. 30 to 120 minims.**
265	17	*for water*	*read alcohol* (***90 per cent.***)
272	29	*for* 1 1/3 grains	*read* 1 grain
274	6	*delete* **Test for Purity.** This solution satisfies the *test for sterility.*	
297	10	*after* **Oculentum Physostigminæ**	*insert* . ***Synonym.*** Oculentum Eserinæ
324	18	*after* when	*insert* dried,
324	19	*after* hours	*insert* (limit of solid paraffins)
326	40	*for* Soft Paraffin, white	*read* White Soft Paraffin
326	41	*for* Soft Paraffin	*read* White Soft Paraffin
352	9	*for* 5	*read* 50
352	36	*before* filter	*insert* previously neutralised to *phenolphthalein,*
352	36	*before alcohol*	*insert* neutralised
375	46	*for* thirty	*read* fifty
379	29	*after* substance	*insert* ;
381	12	*for* the *ether*	*read* freshly redistilled *ether*
381	22	*for* limit	*read* absence
384	2	*for* It contains not less than 98 per cent. of the pods described below.	*read* It contains not more than 2 per cent. of other organic matter.
389	10	*for* 10	*read* 20
389	23	*after* grammes	*insert* , dissolved in 25 millilitres of ***dilute nitric acid FeT.***,

page	line		
391	25	*after* grammes	*insert* , dissolved in 15 millilitres of *dilute nitric acid FeT.*,
394	18	*for* 5	*read* 50
395	17	*for* 5	*read* 50
428	21	*for* 1/120	*read* 1/130
443	14	*after sulphate . . .'.*	*insert* 40 millilitres of the filtrate represents 160 millilitres of the tincture of colchicum being assayed.
445	11	*for* temperture	*read* temperature
450	3	*for* represent	*read* represents
461	16	*for* **Tests**	*read* **Test**
461		*after* line 18	*insert* **Tests for Purity.** Complies with the *tests for sterility.*
468	15	*for Tuberculosis*	*read tuberculosis*
468	34	*for Tuberculosis*	*read tuberculosis*
470	21	*for* Soft Paraffin	*read* White Soft Paraffin
471	8	*for* Soft Paraffin	*read* Yellow Soft Paraffin
473	19	*for* Soft Paraffin, yellow	*read* Yellow Soft Paraffin
485	29	*for extract*	*read extractive*
507	26	*for* ruthenium oxybromide	*read* ammoniated ruthenium hydroxychloride, $Ru_2Cl_4(OH)_2,7NH_3,2H_2O$.
514		*after* line 20	*insert* for N/2 . . . 28·05 grammes KOH
530	36	*for* millilitres	*read* millimetres
535	last	*for* millimetres	*read* millilitres
539	last	*for* No. 118	*read* No. 188
579	27	*for N/10*	*read N/2*
581	2	*for* millilitres	*read* millimetres
581	15	*for* 5	*read* 3
616	31	*for* bilogical	*read* biological
621	6	*for* millitres	*read* millilitres
621	7	*for* represent	*read* represents
621	10	*for* represent	*read* represents
635	13	*for UNDUE*	*read ABNORMAL*
643		*after* line 11	*insert* Abnormal Toxicity, Test for Freedom from . . . *635*
668	49	*for* Undue	*read* Abnormal
708	16	*for* undue	*read* Abnormal
710	33	*for* Undue	*read* Abnormal
711		*delete* line 1	

Additions to the British Pharmacopœia, 1932

Acetarsol
Acidum Ascorbicum
Antitoxinum Œdematiens
Antitoxinum Staphylococcicum
Antitoxinum Vibriosepticum
Argentoproteinum
Bismuthi et Sodii Tartras
Bismuthi Oxychloridum
Calciferol
Calcii Chloridum Hydratum
Calcii Gluconas
Chiniofonum
Ergometrina
Extractum Stramonii Liquidum
Extractum Stramonii Siccum
Ferri Subchloridum Citratum
Histaminæ Phosphas Acidus
Injectio Bismuthi Oxychloridi
Injectio Mersalyli
Liquor Calciferolis
Liquor Iodi Aquosus
Mersalylum
Oleum Iodisatum
Pulvis Vitamini B_1
Serum Antipneumococcicum I
Serum Antipneumococcicum II
Sodii Thiosulphas
Theophyllina
Tryparsamidum

Deletion from the British Pharmacopœia, 1932

Liquor Ergosterolis Irradiati

Monographs of the British Pharmacopœia, 1932, which are amended by the Addendum, 1936

Acetum Scillæ
Acriflavina
Adeps
Adeps Lanæ
Adrenalina
Æther
Aloinum
Alumen
Amylum
Aqua Sterilisata
Atropinæ Sulphas
Belladonnæ Folium
Bismuthi Carbonas
Bismuthum Præcipitatum
Buchu
Calcii Chloridum
Calcii Hydroxidum
Calumba
Carbonei Dioxidum
Cera Flava
Cinchophenum
Digitalis Pulverata
Ergota
Ergotoxinæ Æthanosulphonas
Extractum Belladonnæ Liquidum
Extractum Ergotæ Liquidum
Extractum Hyoscyami Liquidum
Extractum Pituitarii Liquidum
Extractum Senegæ Liquidum
Ferri et Ammonii Citras
Ferrum
Hydrargyri Oxycyanidum
Hydrargyrum cum Creta
Hyoscyamus
Indicarminum
Infusum Digitalis Recens
Injectio Bismuthi
Injectio Bismuthi Salicylatis

Monographs Amended (*continued*)

Injectio Sodii Chloridi et Acaciæ
Insulinum
Iodoformum
Ipecacuanha
Lactosum
Linimentum Belladonnæ
Liquor Adrenalinæ Hydrochloridi
Liquor Cresolis Saponatus
Liquor Ferri Perchloridi
Liquor Iodi Simplex
Liquor Sodii Chloridi Physiologicus
Menthol
Methylis Salicylas
Neoarsphenamina
Oleum Abietis
Oleum Cajuputi
Oleum Chenopodii
Oleum Lavandulæ
Oleum Limonis
Oleum Menthæ Piperitæ
Oleum Morrhuæ
Oleum Myristicæ
Oleum Olivæ
Oleum Rosmarini
Oleum Santali
Oleum Terebinthinæ
Oxygenium
Paraffinum Liquidum
Phenol Liquefactum
Phenolphthaleinum
Plumbi Acetas
Potassii Bicarbonas
Potassii Carbonas
Potassii Citras
Potassii Hydroxidum
Pyroxylinum
Quininæ et Æthylis Carbonas
Rheum
Sapo Animalis
Sapo Durus
Sapo Mollis
Sodii Citras
Sodii Hydroxidum
Sodii Phosphas
Sulpharsphenamina
Thyroideum
Thyroxinsodium
Tinctura Digitalis
Tinctura Ipecacuanhæ
Tinctura Stramonii
Toxinum Diphthericum Detoxicatum
Unguentum Simplex
Unguentum Sulphuris
Valeriana
Zinci Sulphas

GENERAL NOTICES

Page 11,
after last line,
insert

ERRORS OF BIOLOGICAL ASSAYS.

In expressing the limits of error of biological assays the term " limits of error (P = 0·99) " is used. The statements of the errors of these assays are based on the convention that, for practical purposes, a probability of 0·99 is equivalent to certainty. In other words, it has been estimated that the result of the assay will be within the stated limits 99 times out of every 100 times that the assay is made. These limits are given as percentages of the true result. Thus, the statement " limits of error (P = 0·99) 95 and 105 per cent." means that it has been estimated that in 99 assays out of 100 the result will be greater than 95 per cent., and less than 105 per cent., of the true result.

If the error of the test, or its logarithm, is normally distributed, the stated limits of error correspond to the range covered by ± 2·576 times the standard deviation.

The limits of error have been calculated, where possible, from the errors occurring in actual experiments. The errors are, however, liable to vary under conditions which cannot always be precisely defined. Individual workers should estimate the errors from their own data.

The errors of the assays of vitamins have been calculated on the assumption that the response to the standard preparation is equal to the response to the preparation being tested. If the responses are not equal, any device used to allow for this inequality introduces an extra error

which is not included in the stated error. The error due to the inequality can be largely eliminated by so arranging the assay that the preparation being tested is given in two doses, in such a way that one dose has less effect, and the other dose more effect, than the dose of the standard preparation.

MONOGRAPHS

ACETARSOL

[Acetarsol]

Acetarsol

Synonym. Acetarsone.

$CH_3{\cdot}CONH{\cdot}C_6H_3(OH)AsO(OH)_2$ Mol. Wt. 275·0

Acetarsol is 3-acetylamino-4-hydroxyphenylarsonic acid, and may be prepared by the reduction of 3-nitro-4-hydroxyphenylarsonic acid and subsequent acetylation of the amino-acid thereby produced. It contains not less than 27·0 per cent., and not more than 27·4 per cent., of As.

Characters. A white, crystalline powder.

Almost insoluble in cold *water*; moderately soluble in boiling *water*; insoluble in *alcohol* (*95 per cent.*), and in dilute acids; soluble in dilute alkalis.

Tests for Identity. *Melting-point*, 240° to 250°.

Dissolve 1 gramme in 2 millilitres of *solution of sodium hydroxide*, and dilute with *water* to 10 millilitres.

To 2 millilitres of the solution add 2 millilitres of *solution of magnesium ammonio-sulphate*; no precipitate is produced in the cold; boil the solution; a white precipitate is produced.

Heat 2 millilitres of the solution with 2 millilitres of *sulphuric acid* and 2 millilitres of *alcohol* (*95 per cent.*); the odour of ethyl acetate is produced.

Tests for Purity. Dissolve 1 gramme in a mixture of 2 millilitres of *dilute solution of ammonia* and 8 millilitres of *water*, and add 10 millilitres of *solution of magnesium ammonio-sulphate*; no precipitate is produced during thirty minutes (limit of inorganic arsenates).

Dissolve 0·5 gramme in a mixture of 1 millilitre of *solution of sodium hydroxide* and 9 millilitres of *water*, add 10 millilitres of *dilute hydrochloric acid*, and filter. Cool 10 millilitres of the filtrate below 5°, add 2·5 millilitres of a 1 per cent. w/v aqueous solution of *sodium nitrite*, shake, and add 3 millilitres of *solution of sodium hydroxide* and 2·5 millilitres of *solution of β-naphthol*; the colour developed is not deeper than the

colour produced in the following way:—Dissolve 0·01 gramme in a mixture of 15 millilitres of *hydrochloric acid* and 15 millilitres of *water*, boil for five minutes, cool, and dilute with *water* to 100 millilitres. Mix 2·5 millilitres of this solution with 3 millilitres of *dilute hydrochloric acid* and 4·5 millilitres of *water*, cool below 5°, add 2·5 millilitres of a 1 per cent. w/v aqueous solution of *sodium nitrite*, shake, and add 3 millilitres of *solution of sodium hydroxide* and 2·5 millilitres of *solution of β-naphthol* (limit of free amino-acid).

Shake 1 gramme with 10 millilitres of *water*, and filter; 5 millilitres of the filtrate complies with the *limit test for chlorides*.

Loses, when dried at 100° for four hours, not more than 0·5 per cent. of its weight, and leaves, on incineration, not more than 0·2 per cent. of residue.

Assay. Carry out the Assay for Arsenic as described under 'Tryparsamidum'. Each millilitre of *N/10 iodine* is equivalent to 0·003747 gramme of As.

DOSES

Metric.	Imperial.
0·06 to 0·25 gramme.	1 to 4 grains.

ACETUM SCILLÆ
Vinegar of Squill

Page 15, line 4,

delete ", and filter while hot".

ACIDUM ASCORBICUM
[Acid. Ascorb.]
Ascorbic Acid

Synonym. Vitamin C.

$C_6H_8O_6$ Mol. Wt. 176·1

Ascorbic Acid, the enolic form of 3-keto-*l*-gulofuranolactone, may be obtained from the ripe fruit of *Capsicum annuum* Linn. and other vegetable sources, or by synthesis. It contains not less than 98 per cent. of $C_6H_8O_6$.

Characters. Minute colourless crystals; odourless; taste, acid, resembling that of lemon juice.

Readily soluble in *water*; less soluble in *alcohol (95 per cent.)*, in *methyl alcohol*, and in *acetone*; insoluble in *ether*, and in *light petroleum*.

Tests for Identity and Purity. An aqueous solution is acid to *litmus*.

An aqueous solution liberates carbon dioxide from *solution of sodium bicarbonate*.

An aqueous solution decolorises *solution of 2 : 6-dichlorophenol-indophenol*.

An aqueous solution reduces *solution of potassio-cupric tartrate*, producing a yellowish precipitate.

An aqueous solution reduces *solution of potassium permanganate* immediately, producing a faintly brown or colourless solution.

An aqueous solution reduces *solution of silver nitrate* immediately, producing a black precipitate.

Melting-point, 190° to 192°, with decomposition; *specific rotation* in a 2 per cent. w/v aqueous solution, + 22° to + 23°, in a 2 per cent. w/v solution in *methyl alcohol*, + 50° to + 51°, in a 2 per cent. w/v solution in a mixture of 12 millilitres of *N/1 sodium hydroxide* with a sufficient quantity of *water* to produce 100 millilitres, + 112° to + 115°; *ultra-violet absorption* in a 0·002 per cent. w/v aqueous solution of *p*H 3, or less, at 245mμ, 550.

Assay. Dissolve about 0·04 gramme, accurately weighed, in a mixture of 5 millilitres of *water* and 5 millilitres of *dilute sulphuric acid*, and titrate with *N/100 iodine*, using *mucilage of starch* as indicator. Each millilitre of *N/100 iodine* is equivalent to 0·00088 gramme of $C_6H_8O_6$.

Storage. Crystalline Ascorbic Acid is stable, when kept in a glass bottle. Solutions of Ascorbic Acid, especially if alkaline, deteriorate rapidly in contact with air.

DOSES

Metric.	Imperial.
Prophylactic (daily)	
0·025 to 0·05 gramme.	**$^2/_5$ to $^4/_5$ grain.**
(500 to 1000 Units).	
Therapeutic (daily)	
0·1 to 0·25 gramme.	**1$^1/_2$ to 4 grains.**
(2000 to 5000 Units).	

Ascorbic Acid possesses antiscorbutic properties and, if tested by the *biological assay of antiscorbutic vitamin* (*vitamin C*), contains in 1 gramme 20,000 *Units of antiscorbutic activity* (*vitamin C*).

The antiscorbutic activity of a preparation containing vitamin C, for which the chemical assay is not applicable, is determined in relation to the Standard Preparation of antiscorbutic vitamin (vitamin C) by the *biological assay of antiscorbutic vitamin* (*vitamin C*), and is expressed in Units per gramme.

ACRIFLAVINA

Acriflavine

Pages 35 and 36,

delete this monograph;

insert

ACRIFLAVINA

[Acriflavin.]

Acriflavine

Acriflavine is a mixture of the hydrochlorides of 2 : 8-diamino-10-methylacridinium chloride and 2 : 8-diaminoacridine, and contains approximately one-third of its weight of diaminoacridine dihydrochloride. It may be prepared by the partial methylation of diacetyldiaminoacridine and subsequent hydrolysis of the product with hydrochloric acid.

Characters. An orange-red to red, crystalline powder; odourless; taste, acid.

Soluble in about 3 parts of *water*; this solution may precipitate on dilution, or on standing. Soluble in about 500 parts of *physiological solution of sodium chloride*. Soluble in *alcohol* (*90 per cent.*); almost insoluble in *ether*, and in *chloroform*; soluble in *glycerin*; almost insoluble in fixed and volatile oils, and in *liquid paraffin*.

Tests for Identity. 0·04 gramme, dissolved in 10 millilitres of *water*, forms a deep orange-coloured fluorescent solution, which responds to the following tests:—

2 millilitres, diluted with about twice its volume of *water*, gives a red colour on the addition of a few drops of *solution of methyl orange*.

2 millilitres yields a bulky yellow precipitate on the addition of a 10 per cent. w/v aqueous solution of *sodium salicylate* (distinction from fluorescein).

5 millilitres gives a brownish precipitate on the addition of a few drops of *solution of formaldehyde* and 5 millilitres of a 10 per cent. w/v aqueous solution of *sodium nitrite*. When the mixture is allowed to stand for five minutes and filtered, the filtrate is cherry-red in colour (distinction from unmethylated diaminoacridine compounds).

Yields the *reactions* characteristic of chlorides.

Tests for Purity. 1 gramme, dissolved in 50 millilitres of *water*

at 30°, forms a clear solution, which remains clear and free from sediment on standing in the dark at 15° to 20° for twenty-four hours.

0·2 gramme, dissolved in 100 millilitres of a 0·9 per cent. w/v aqueous solution of *sodium chloride* at 30°, forms a clear solution, which remains clear and free from sediment on standing in the dark at 15° to 20° for twenty-four hours.

Moisten 1 gramme with *sulphuric acid*, ignite gently, again moisten with *sulphuric acid*, and re-ignite; the residue weighs not more than 0·01 gramme.

DOSES

Metric.	Imperial.
0·03 to 0·1 gramme.	1/2 to 1 1/2 grains.

ADEPS

Lard

Page 37, lines 7–9,

delete "; and, after being filtered and acidified with *nitric acid*, does not yield any *reaction* with *solution of silver nitrate* (absence of chlorides)";

insert "Boil 1 gramme with 20 millilitres of *alcohol* (*90 per cent.*) under a reflux condenser for five minutes, cool, add 40 millilitres of *water* and 0·5 millilitre of *nitric acid*, filter, and to the filtrate add 5 drops of a 1 per cent. w/v solution of *silver nitrate* in *alcohol* (*90 per cent.*); the turbidity, if any, is not greater than that produced by adding 5 drops of a 1 per cent. w/v solution of *silver nitrate* in *alcohol* (*90 per cent.*) to a mixture of 0·5 millilitre of *N/50 hydrochloric acid*, 20 millilitres of *alcohol* (*90 per cent.*), 40 millilitres of *water* and 0·5 millilitre of *nitric acid*, the liquids being examined after an interval of five minutes (limit of chlorides).".

ADEPS LANÆ

Wool Fat

Page 38,

delete lines 5–12;

insert "Complies with the test for limit of chlorides described under 'Adeps'.".

ADRENALINA

Adrenaline

Page 38,

after line 35,

insert "*CAUTION—In any part of the British Empire in which Adrenaline (Epinèphrine) is controlled by law, care must be taken that the provisions of such law are duly complied with.* (*See page 12.*)".

ÆTHER

Ether

Page 40, line 9,

delete "and not more than *p*H 5·1,".

after line 22,

insert "Complies with the test for methyl alcohol described under 'Æther Anæstheticus'.".

ALOINUM

Aloin

Page 48,

delete lines 21–26;

insert "Place 1 gramme in a stoppered flask with 120 millilitres of *water* at 25°, and shake frequently during two hours, maintaining the temperature at 25° throughout; filter through a Gooch crucible, which has been prepared with asbestos, dried at 100° and tared; wash the residue on the filter with 25 millilitres of *water*, and dry at 100°; the residue weighs not more than 0·015 gramme.".

ALUMEN

Alum

Page 49,

delete lines 26–28;

insert "Dissolve 1 gramme in 1000 millilitres of *ammonia-free water*; to 10 millilitres of the solution add 40 millilitres of

ammonia-free water and 2 millilitres of *alkaline solution of potassio-mercuric iodide*; any colour produced is not deeper than that given by 1 millilitre of *dilute solution of ammonium chloride* (*Nessler's*) in 50 millilitres of *ammonia-free water*, to which 2 millilitres of *alkaline solution of potassio-mercuric iodide* has been added (limit of ammonium salts).".

AMYLUM

Starch

Page 55, last line,

after " Linn.",
insert " or of rice, *Oryza sativa* Linn.".

Page 56, line 2,

after " odourless.",
insert " *Maize Starch.*".

after line 5,

insert " *Rice Starch.* Consists of single and compound grains; single grains, polyhedral, usually from 5 to 8 microns in diameter, and sometimes exhibiting a minute central hilum; compound grains, ovate, usually from 12 to 30 microns in length and from 7 to 20 microns in width, and containing from 2 to 150 component grains.".

ANTITOXINUM ŒDEMATIENS

[Antitox. Œdemat.]

Gas-gangrene Antitoxin (œdematiens)

CAUTION.—In any part of the British Empire in which Gas-gangrene Antitoxin (œdematiens) is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

Gas-gangrene Antitoxin (œdematiens) is serum, or a preparation from serum, containing the antitoxic globulins which have the specific power of neutralising the toxin formed by *Clostridium œdematiens.*

It is prepared by separating the serum from the blood of animals, which have been immunised by graded injections of the sterile filtrate from a culture of *Clostridium œdematiens* in a fluid medium. The serum may be used in the liquid form, or may be dried. The antitoxic globulins may be obtained from the serum by fractional precipitation, and the precipitate may be used either in solution, or dried. The final sterile product, whether serum, dried serum, solution of antitoxic globulins, or dried antitoxic globulins, is distributed in sterilised glass containers, which are sealed so as to exclude bacteria. An antiseptic may be added to the liquid forms.

Characters. The liquid serum is yellow or yellowish-brown. The solution of the antitoxic globulins is yellowish-brown or greenish-yellow. Both liquid forms are initially transparent, but acquire with age a faint opalescence. They are almost odourless, except for the odour of any antiseptic which may have been added. The solid forms are yellowish-white powders, or yellowish-brown flakes. When dissolved in 10 parts of *water*, they resemble the liquid forms in colour and appearance. The liquid serum does not contain more than 10 per cent. w/v of solid matter. The solution of antitoxic globulins does not contain more than 20 per cent. w/v of solid matter. The solid forms do not contain antiseptic, or other added substance.

Test for Identity. It renders the toxin formed by *Clostridium œdematiens* harmless to animals.

Tests for Purity. All forms comply with the *tests for sterility*. All forms comply with the *tests for freedom from abnormal toxicity*.

Assay. Determine the potency in relation to the Standard Preparation of gas-gangrene antitoxin (œdematiens) by the *biological assay of gas-gangrene antitoxin* (*œdematiens*), and express it in Units per millilitre for liquid preparations, and in Units per gramme for solid preparations.

Storage. Gas-gangrene Antitoxin (œdematiens) should be kept at as low a temperature as possible above its freezing-point. The number of Units placed in each container must be sufficient to ensure that the number stated on the label is still present at the end of the period during which the preparation is intended to be used.

Labelling. The label or wrapper on the package, or the label on the container, states:—(1) whether the product is serum, dried serum, solution of antitoxic globulins, or dried antitoxic

globulins; (2) the date after which the preparation is not intended to be used.

The label on the container states:—(1) the minimum total number of Units in the container; (2) either (*a*) the number of Units in 1 millilitre, or in 1 gramme, or (*b*) the total number of millilitres of liquid, or grammes of dried product, in the container.

DOSES

By injection.

Prophylactic 20,000 Units.
Therapeutic 50,000 to 100,000 Units.

ANTITOXINUM STAPHYLOCOCCICUM

[Antitox. Staphylococc.]

Staphylococcus Antitoxin

CAUTION.—In any part of the British Empire in which Staphylococcus Antitoxin is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

Staphylococcus Antitoxin is serum, or a preparation from serum, containing the antitoxic globulins which have the specific power of neutralising the toxin formed by certain strains of *Staphylococcus*.

It is prepared by separating the serum from the blood of animals, which have been immunised by graded injections of the sterile filtrate from a culture of *Staphylococcus pyogenes* in a suitable medium. The serum may be used in the liquid form, or may be dried. The antitoxic globulins may be obtained from the serum by fractional precipitation, and the precipitate may be used either in solution, or dried. The final sterile product, whether serum, dried serum, solution of antitoxic globulins, or dried antitoxic globulins, is distributed in sterilised glass containers, which are sealed so as to exclude bacteria. An antiseptic may be added to the liquid forms.

Characters. The liquid serum is yellow or yellowish-brown. The solution of the antitoxic globulins is yellowish-brown or greenish-yellow. Both liquid forms are initially transparent, but acquire

with age a faint opalescence. They are almost odourless, except for the odour of any antiseptic which may have been added. The solid forms are yellowish-white powders, or yellowish-brown flakes. When dissolved in 10 parts of *water* they resemble the liquid forms in colour and appearance. The liquid serum does not contain more than 10 per cent. w/v of solid matter. The solution of antitoxic globulins does not contain more than 20 per cent. w/v of solid matter. The solid forms do not contain antiseptic, or other added substance.

Test for Identity. It renders the toxin formed by certain strains of *Staphylococci* harmless to animals, and neutralises its lytic action, when tested in vitro, on the red blood corpuscles of the rabbit.

Tests for Purity. All forms comply with the *tests for sterility*. All forms comply with the *tests for freedom from abnormal toxicity*.

Assay. Determine the potency in relation to the Standard Preparation of staphylococcus antitoxin by the *biological assay of staphylococcus antitoxin*, and express it in Units per millilitre for liquid preparations, and in Units per gramme for solid preparations.

Storage. Staphylococcus Antitoxin should be kept at as low a temperature as possible above its freezing-point. The number of Units placed in each container must be sufficient to ensure that the number stated on the label is still present at the end of the period during which the preparation is intended to be used.

Labelling. The label or wrapper on the package, or the label on the container, states:—(1) whether the product is serum, dried serum, solution of antitoxic globulins, or dried antitoxic globulins; (2) the date after which the preparation is not intended to be used.

The label on the container states:—(1) the minimum total number of Units in the container; (2) either (*a*) the number of Units in 1 millilitre, or in 1 gramme, or (*b*) the total number of millilitres of liquid, or grammes of dried product, in the container.

DOSES

By injection.

5000 to 20,000 Units.

ANTITOXINUM VIBRIOSEPTICUM

[Antitox. Vibrioseptic.]

Gas-gangrene Antitoxin (vibrion septique)

CAUTION.—In any part of the British Empire in which Gas-gangrene Antitoxin (vibrion septique) is controlled by

law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

Gas-gangrene Antitoxin (vibrion septique) is serum, or a preparation from serum, containing the antitoxic globulins which have the specific power of neutralising the toxin formed by the *Clostridium*, commonly known as Vibrion Septique.

It is prepared by separating the serum from the blood of animals, which have been immunised by graded injections of the sterile filtrate from a culture of the *Clostridium*, commonly known as Vibrion Septique, in a fluid medium. The serum may be used in the liquid form, or may be dried. The antitoxic globulins may be obtained from the serum by fractional precipitation, and the precipitate may be used either in solution, or dried. The final sterile product, whether serum, dried serum, solution of antitoxic globulins, or dried antitoxic globulins, is distributed in sterilised glass containers, which are sealed so as to exclude bacteria. An antiseptic may be added to the liquid forms.

Characters. The liquid serum is yellow or yellowish-brown. The solution of the antitoxic globulins is yellowish-brown or greenish-yellow. Both liquid forms are initially transparent, but acquire with age a faint opalescence. They are almost odourless, except for the odour of any antiseptic which may have been added. The solid forms are yellowish-white powders, or yellowish-brown flakes. When dissolved in 10 parts of *water* they resemble the liquid forms in colour and appearance. The liquid serum does not contain more than 10 per cent. w/v of solid matter. The solution of antitoxic globulins does not contain more than 20 per cent. w/v of solid matter. The solid forms do not contain antiseptic, or other added substance.

Test for Identity. It renders the toxin formed by the *Clostridium*, commonly known as Vibrion Septique, harmless to animals.

Tests for Purity. All forms comply with the *tests for sterility*. All forms comply with the *tests for freedom from abnormal toxicity*.

Assay. Determine the potency in relation to the Standard Preparation of gas-gangrene antitoxin (vibrion septique) by the *biological assay of gas-gangrene antitoxin (vibrion septique)*, and

express it in Units per millilitre for liquid preparations, and in Units per gramme for solid preparations.

Storage. Gas-gangrene Antitoxin (vibrion septique) should be kept at as low a temperature as possible above its freezing-point. The number of Units placed in each container must be sufficient to ensure that the number stated on the label is still present at the end of the period during which the preparation is intended to be used.

Labelling. The label or wrapper on the package, or the label on the container, states:—(1) whether the product is serum, dried serum, solution of antitoxic globulins, or dried antitoxic globulins; (2) the date after which the preparation is not intended to be used.

The label on the container states:—(1) the minimum total number of Units in the container; (2) either (*a*) the number of Units in 1 millilitre, or in 1 gramme, or (*b*) the total number of millilitres of liquid, or grammes of dried product, in the container.

DOSES

By injection.

Prophylactic 5000 Units.
Therapeutic 10,000 to 20,000 Units.

AQUA STERILISATA

Sterilised Water

Page 70,

delete this monograph;

insert

AQUA STERILISATA

[Aq. Steril.]

Sterilised Water

Distil potable water from a glass still, or a still in which the distillate does not come in contact with copper, which has been cleansed immediately before distillation. Reject the first portion of the distillate and collect the remainder in a sterilised neutral glass container. Close the container so as to exclude bacteria, either by inserting a plug of sterile non-absorbent cotton-wool wrapped in gauze, or

by fusion of the glass, or by some equally effective method, and immediately sterilise by *heating in an autoclave.*

Sterilised water kept in a container which is closed with cotton-wool is used within one month after its preparation. If kept in a container which is sealed by fusion of the glass, or by some equally effective method, it may be stored for a longer period.

If the whole of the contents of a container is not used when the container is opened, the remainder may be stored as described above, provided that the container is immediately both closed again so as to exclude bacteria and sterilised by *heating in an autoclave.*

Emergency Method. If an autoclave is not available place the water, freshly distilled as described, in a sterilised neutral glass container, close the container so as to exclude bacteria by inserting a plug of sterile non-absorbent cotton-wool wrapped in gauze, and boil for thirty minutes. Sterilised water prepared by the emergency method is used within twenty-four hours of its preparation.

Tests for Purity. Complies with the Tests for Purity described under 'Aqua Destillata'.

ARGENTOPROTEINUM

[Argentoprot.]

Silver Protein

Synonyms. Argentum-Proteinicum Forte: Strong Protein Silver: Silver Proteinate.

Silver Protein is a compound of silver and protein, which may be prepared by the action of a silver compound on gelatin in the presence of alkali. It contains not less than 7·5 per cent., and not more than 8·5 per cent., of Ag.

Characters. A brown powder; odourless; somewhat hygroscopic.

Slowly soluble in about 2 parts of *water*, forming a dark brown solution; almost insoluble in *alcohol (95 per cent.)*, in *ether*, and in *chloroform.*

Tests for Identity. Chars when heated, and, on complete incinera-

tion, leaves a greyish-white residue, which yields the *reactions* characteristic of silver.

When *test-solution of ferric chloride* is added to a 1 per cent. w/v aqueous solution, the dark colour is discharged, and the solution becomes opalescent on standing.

When *test-solution of mercuric chloride* is added to a 1 per cent. w/v aqueous solution, a white precipitate is formed, and the liquid becomes colourless or almost colourless.

To 5 millilitres of a 2 per cent. w/v aqueous solution add 5 millilitres of *solution of sodium hydroxide*, dilute with 10 millilitres of *water*, add 2 millilitres of a 2 per cent. w/v aqueous solution of *copper sulphate*, and allow to stand for a few minutes; a violet colour is produced.

Test for Purity. Shake 1 gramme with 10 millilitres of *alcohol (90 per cent.)*, filter, and add 2 millilitres of *dilute hydrochloric acid*; no turbidity is produced (limit of silver salts).

Assay. Ignite about 2 grammes, accurately weighed, at first gently and afterwards strongly until all carbonaceous matter is destroyed. Dissolve the residue in 10 millilitres of *nitric acid*, heat until no more nitrous fumes are evolved, dilute with *water* to 100 millilitres, and titrate with *N/10 ammonium thiocyanate*, using *solution of ferric ammonium sulphate* as indicator. Each millilitre of *N/10 ammonium thiocyanate* is equivalent to 0·01079 gramme of Ag.

Storage. Silver Protein should be kept in a well-closed container, protected from light.

NOTE.—Solutions of Silver Protein should be freshly prepared and dispensed in amber-coloured bottles.

ATROPINÆ SULPHAS

Atropine Sulphate

Page 76, line 13,

delete "105°";
insert "136°".

BELLADONNÆ FOLIUM

Belladonna Leaf

Page 84, line 10,

after "*dilute solution of ammonia*",
insert "mixed with 2 millilitres of *water*,".

Page 84, line 32,
before "shake",
insert ", without delay,".
line 33,
after "effected",
insert ", carrying out the extraction as rapidly as possible".

BISMUTHI CARBONAS

Bismuth Carbonate

Page 89, line 28,
delete "89";
insert "90".
line 29,
delete "91";
insert "92".

BISMUTHI ET SODII TARTRAS

[Bism. et Sod. Tart.]

Sodium Bismuthyltartrate

Synonym. Bismuth Sodium Tartrate.

Sodium Bismuthyltartrate may be obtained by the interaction of bismuth hydroxide and sodium acid tartrate. It contains not less than 35 per cent., and not more than 42 per cent., of Bi.

Characters. A white powder, or slightly yellow scales.
Soluble in less than 1 part of *water*.

Tests for Identity. Yields the *reactions* characteristic of bismuth, and of sodium, and, after removal of the bismuth, the *reactions* characteristic of tartrates.
An aqueous solution is neutral to *litmus*.

Tests for Purity. Ignite 4 grammes, add a few drops of *nitric acid*, re-ignite, dissolve the residue in 4 millilitres of *nitric acid*, evaporate the solution to half its volume, dilute to 100 millilitres with *water*, and filter; 5 millilitres of the filtrate complies with the limit tests for lead, and for copper, described under 'Bismuthi Carbonas'.
Arsenic limit, 2 parts per million.

Assay. Dissolve about 0·5 gramme, accurately weighed, in 50 millilitres of *water*, and add *nitric acid* gradually until a precipitate is produced. Complete the Assay as directed under 'Bismuthum Præcipitatum', commencing with the words 'Add just sufficient nitric acid to redissolve . . .'. Each gramme of the residue is equivalent to 0·6875 gramme of Bi.

Sterilisation of a Solution. A solution of Sodium Bismuthyltartrate for injection is sterilised by *heating in an autoclave*, or by *Tyndallisation*, or by *filtration*.

DOSES

Metric.	Imperial.
By intramuscular injection.	
0·06 to 0·2 gramme.	1 to 3 grains.

BISMUTHI OXYCHLORIDUM

[Bism. Oxychlor.]

Bismuth Oxychloride

Synonym. Bismuth Subchloride.

Bismuth Oxychloride is a basic salt of varying composition, obtained by the interaction of solutions of bismuth nitrate and sodium chloride or hydrochloric acid. It contains not less than 79 per cent., and not more than 81 per cent., of Bi, and not less than 12·5 per cent. of Cl.

Characters. A white or nearly white, amorphous or finely crystalline powder; odourless; tasteless. Stable in air.

Insoluble in *water*; soluble in *dilute hydrochloric acid*.

Tests for Identity. Yields the *reactions* characteristic of bismuth, and of chlorides.

Tests for Purity. Complies with the tests for limit of lead, copper, and sulphates, described under 'Bismuthi Carbonas'.

Mix 0·5 gramme with 10 millilitres of *water*; add 5 millilitres of *solution of indigo carmine*, followed rapidly by 15 millilitres of *nitrogen-free sulphuric acid* in two approximately equal portions. Boil, and set aside for one minute; the blue colour is not entirely discharged (limit of nitrates).

Arsenic limit, 2 parts per million.

Assay. *For bismuth.* Carry out the Assay as described under 'Bismuthum Præcipitatum'. Each gramme of the residue is equivalent to 0·6875 gramme of Bi.

For chlorine. Dissolve about 1 gramme, accurately weighed, in a mixture of 10 millilitres of *nitric acid* with 25 millilitres

of *water*, add 50 millilitres of *N/10 silver nitrate*, boil, filter, cool, and titrate with *N/10 ammonium thiocyanate*, using *solution of ferric ammonium sulphate* as indicator. Each millilitre of *N/10 silver nitrate* is equivalent to 0·003546 gramme of Cl.

Storage. Bismuth Oxychloride should be protected from light.

Preparation. Injectio Bismuthi Oxychloridi.

DOSES

Metric.	Imperial.
0·6 to 2 grammes.	10 to 30 grains.

By intramuscular injection.

0·1 to 0·2 gramme.	$1^1/_2$ to 3 grains.

BISMUTHUM PRÆCIPITATUM

Precipitated Bismuth

Page 91,

delete lines 23–25;

insert "**Tests for Purity.** Dissolve 3 grammes in 6 millilitres of warm *nitric acid*, and pour the solution into 100 millilitres of *water*; filter, wash, and evaporate the filtrate and washings to 30 millilitres, and again filter. To 5 millilitres of the filtrate add a slight excess of *dilute solution of ammonia*; a white precipitate is produced, and the supernatant liquid shows no bluish tint (limit of copper).

Suspend 1 gramme in 6 millilitres of *hydrochloric acid*, and add 1 gramme of *potassium chlorate*. Warm until solution is complete, adding more *potassium chlorate*, if necessary. Boil nearly to dryness to ensure that all the chlorine is expelled. Cool, and make up to 6 millilitres with *hydrochloric acid*. Add 2 drops of *solution of potassium iodide*; no turbidity or opalescence is produced (limit of silver).

0·25 gramme, dissolved in 5 millilitres of *nitric acid*, complies with the *limit test for chlorides*.

Arsenic limit, 10 parts per million.".

BUCHU

Buchu

Page 93, line 21,

after "*Ash*, not more than 5 per cent.",

insert "*Alcohol (25 per cent.)-soluble extractive*, not less than 20 per cent.".

CALCIFEROL

[Calciferol]

Calciferol

$C_{28}H_{43}OH$ . . . . Mol. Wt. 396·3

Calciferol may be prepared by the ultra-violet irradiation of ergosterol in a suitable solvent. The product of the irradiation, after removal of the solvent, is dissolved in Alcohol (95 per cent.) or other suitable organic solvent, and strongly cooled. The unchanged ergosterol, which separates, is removed by filtration, and the solvent is removed from the filtrate by evaporation under reduced pressure; the residue is dissolved in *pyridine*, and warmed with a solution of *3 : 5-dinitrobenzoyl chloride* in *pyridine*. Distilled Water is added; the mixture of 3 : 5-dinitrobenzoates, which separates, is thoroughly washed with Distilled Water, and recrystallised from Acetone until the *specific rotation* of the crystals in solution in *benzene* is (sodium light) + 57° to + 60°, (mercury light) + 68·5° to + 72·5°. The calciferyl 3 : 5-dinitrobenzoate is then hydrolysed by boiling in alcoholic solution with a slight excess of sodium hydroxide, Distilled Water is added, and the calciferol, which crystallises, is recrystallised from methyl alcohol, or other suitable solvent. It contains in 1 milligram 40,000 *Units of antirachitic activity* (*vitamin D*).

Characters. Colourless acicular crystals; odourless.

Insoluble in *water*; readily soluble in *alcohol* (*95 per cent.*), in *ether*, in *chloroform*, and in *acetone*; soluble in 50 to 100 parts of vegetable oils.

Tests for Identity. Dissolve 0·5 gramme in about 1 millilitre of dry *pyridine*; dissolve 0·5 gramme of *3 : 5-dinitrobenzoyl chloride* in about 2 millilitres of dry *pyridine* by warming on a water-bath; mix the solutions, and warm on a water-bath for ten minutes. Add 5 millilitres of *water* to the hot solution, filter, and wash the precipitate with *water*. Dissolve the precipitate in about 10 millilitres of hot *acetone*, cool, and allow to stand for a short time. Collect the calciferyl 3 : 5-dinitrobenzoate on a filter, wash with a little cold *acetone*, and dry in a vacuum desiccator: *melting-point* of calciferyl 3 : 5-dinitrobenzoate, 147° to 149°; *specific rotation* of calciferyl 3 : 5-dinitrobenzoate in solution in *benzene* (mercury light), + 68·5° to + 72·5°.

Melting-point, the substance being heated in an evacuated sealed capillary tube, 115° to 119°; *specific rotation*, in a freshly-prepared 4 per cent. w/v solution in *dehydrated alcohol* (sodium light), + 102·5° to + 107·5°, (mercury light), + 122·5° to + 128·5°; *ultra-violet absorption* in *dehydrated alcohol* at 265mμ, not below 460.

Test for Purity. Treat a 1 per cent. w/v solution in *alcohol* (*90 per cent.*) with an equal volume of a 1 per cent. solution of *digitonin* in *alcohol* (*90 per cent.*), and allow to stand for twelve hours; no precipitate is produced (absence of ergosterol).

Assay. Determine the antirachitic activity in relation to the Standard Preparation of antirachitic vitamin (vitamin D) by the *biological assay of antirachitic vitamin* (*vitamin D*), and express the result in Units per milligram.

Storage. Calciferol should be kept in hermetically sealed glass containers, from which air has been evacuated or replaced by an inert gas, protected from light, and stored in a cool place.

Preparation. Liquor Calciferolis.

DOSES

Metric.	Imperial.
Prophylactic (daily) for an infant	
0·025 to 0·05 milligram. (1000 to 2000 Units).	$^1/_{2400}$ to $^1/_{1200}$ grain.
Therapeutic (daily) for an infant	
0·05 to 0·075 milligram. (2000 to 3000 Units).	$^1/_{1200}$ to $^1/_{800}$ grain.

CALCII CHLORIDUM
Calcium Chloride

Page 97,

delete lines 42–45;

insert "When Calcium Chloride is prescribed for injection, twice the prescribed amount of Hydrated Calcium Chloride shall be dispensed.".

CALCII CHLORIDUM HYDRATUM
[Calc. Chlorid. Hydrat.]
Hydrated Calcium Chloride

$CaCl_2,6H_2O$ . . . Mol. Wt. 219·1

Hydrated Calcium Chloride may be obtained by neutralising hydrochloric acid with calcium carbonate, and crystallis-

ing the product. It contains not less than 98 per cent., and not more than the equivalent of 102 per cent., of $CaCl_2, 6H_2O$.

Characters. Colourless crystals; odourless; taste, slightly bitter. Very deliquescent.

Soluble in 0·25 part of *water*, and in 0·95 part of *alcohol (90 per cent.)*.

Tests for Identity. Heated in a dry tube, it melts and water is expelled.

Yields the *reactions* characteristic of calcium, and of chlorides.

Tests for Purity. A solution of 5 grammes in 20 millilitres of *water* is clear and colourless. This solution requires for neutralisation not more than 0·1 millilitre of either *N/10 hydrochloric acid* or *N/10 sodium hydroxide, solution of bromothymol blue* being used as indicator (limit of free alkali and free acid).

Dissolve 5 grammes in 20 millilitres of *water* and 1 millilitre of *hydrochloric acid*; add a slight excess of *dilute solution of ammonia*, filter, and wash; the residue, after being dried and gently ignited, weighs not more than 0·001 gramme (limit of aluminium, iron, phosphate, and matter insoluble in hydrochloric acid).

5 grammes complies with the *limit test for sulphates*.

Arsenic limit, 2 parts per million. *Lead limit*, 10 parts per million.

Assay. Dissolve about 5 grammes, accurately weighed, in sufficient *water* to produce 250 millilitres; dilute 20 millilitres of this solution with 50 millilitres of *water*, and titrate with *N/10 silver nitrate*, using *solution of potassium chromate* as indicator. Each millilitre of *N/10 silver nitrate* is equivalent to 0·01095 gramme of $CaCl_2,6H_2O$.

Storage. Hydrated Calcium Chloride should be kept in a well-closed container.

Sterilisation of a Solution. A Solution of Hydrated Calcium Chloride for injection is sterilised by *heating in an autoclave*, or by *Tyndallisation*.

DOSES

Metric.	Imperial.
By intramuscular injection.	
0·06 to 0·2 gramme.	**1 to 3 grains.**
By intravenous injection.	
0·6 to 2 grammes.	**10 to 30 grains.**

CALCII GLUCONAS

[Calc. Glucon.]

Calcium Gluconate

$[CH_2OH{\cdot}(CHOH)_4{\cdot}COO]_2Ca,H_2O$ . . Mol. Wt. 448·3

Calcium Gluconate is the normal calcium salt of gluconic acid. It contains not less than 99 per cent., and not more than the equivalent of 104 per cent., of $C_{12}H_{22}O_{14}Ca,H_2O$.

Characters. A white, crystalline or granular powder; odourless; tasteless.

Slowly soluble in 30 parts of *water* at 25°; soluble in about 5 parts of boiling *water*; insoluble in *dehydrated alcohol*, in *ether*, and in *chloroform*.

Tests for Identity. A 2 per cent. w/v solution in *water* is neutral to *litmus*.

Yields the *reactions* characteristic of calcium.

To 1 millilitre of a 2 per cent. w/v solution in *water* add 1 drop of *test-solution of ferric chloride*; a yellow colour is produced.

To 5 millilitres of a warm 10 per cent. w/v solution in *water* add 0·65 millilitre of *glacial acetic acid* and 1 millilitre of freshly distilled *phenylhydrazine*, and heat on a water-bath for thirty minutes; allow to cool and scratch the inner surface of the tube until crystals of gluconic acid phenylhydrazide begin to form. Filter the mass, dissolve it in 10 millilitres of hot *water*, add a small amount of *decolourising charcoal*, and filter. Allow the filtrate to cool, and scratch the inner surface of the tube; white crystals are obtained, *melting-point*, 200° to 202° with decomposition.

Tests for Purity. Dissolve 0·5 gramme in 10 millilitres of hot *water*, add 2 millilitres of *dilute hydrochloric acid*, and boil for about two minutes. Cool, add 15 millilitres of *solution of sodium carbonate*, allow to stand for five minutes, and filter. Add 5 millilitres of the clear filtrate to about 2 millilitres of *solution of potassio-cupric tartrate*, and boil for one minute; no red precipitate is formed (absence of dextrose, and of sucrose).

0·5 gramme complies with the *limit test for chlorides*.

1·0 gramme complies with the *limit test for sulphates*.

Arsenic limit, 5 parts per million. *Lead limit*, 10 parts per million.

Assay. Dissolve about 1 gramme, accurately weighed, in 100 millilitres of *water* and 2 millilitres of *hydrochloric acid*, add a slight excess of *dilute solution of ammonia*, boil, and add 50 millilitres of *solution of ammonium oxalate*; heat on a water-

bath for one hour, and filter off the precipitate; wash, dry, moisten with *sulphuric acid*, ignite gently, and weigh the residue. 1 gramme of the residue is equivalent to 3·293 grammes of $C_{12}H_{22}O_{14}Ca,H_2O$.

Storage. Calcium Gluconate should be kept in a well-closed container.

DOSES

Metric.	Imperial.
2 to 4 grammes.	30 to 60 grains.

CALCII HYDROXIDUM

Calcium Hydroxide

Page 98, line 16,

delete "and filter";

insert "filter and wash the residue with *water*".

line 17,

delete "0·01";

insert "0·02".

line 21,

delete "0·5";

insert "0·25".

delete "2·5";

insert "1·5".

CALUMBA

Calumba

Page 101, line 19,

after "*Ash*, not more than 9 per cent.",

insert "*Alcohol* (*60 per cent.*)-*soluble extractive*, not less than 12 per cent.".

CARBONEI DIOXIDUM

Carbon Dioxide

Page 104,

delete lines 38–40, and

Page 105,

delete lines 1–7;

insert "**Tests for Purity.** For the following tests the reagent is placed in a 100-millilitre cylinder, which has a height of about 20 centimetres and is closed with a stopper, containing an inlet tube, which has a bore not exceeding 0·5 millimetre and passes to the bottom of the cylinder, and an exit tube. The gas is passed through the reagent at a rate of about 1 litre, measured at normal temperature and pressure, in fifteen minutes.

Pass a volume equivalent to 500 millilitres, measured at normal temperature and pressure, through 50 millilitres of *solution of sodium bicarbonate*, and then through 80 millilitres of *water* to which 4 drops of *solution of methyl orange* has been added. Then pass a volume equivalent to 500 millilitres, measured at normal temperature and pressure, directly through one-half of this methyl orange solution; the colour of the solution does not differ from that of the other half of the methyl orange solution (limit of acid, and of sulphur dioxide).

Pass a volume equivalent to 1000 millilitres, measured at normal temperature and pressure, through a mixture of 25 millilitres of *solution of silver nitrate*, 7 millilitres of *dilute solution of ammonia* and 20 millilitres of *water*; no turbidity or darkening is produced (limit of phosphine, of hydrogen sulphide, and of organic reducing substances).".

CERA FLAVA

Yellow Beeswax

Page 113, line 15,

delete "4·0";

insert "4·2".

CHINIOFONUM

[Chiniofon.]

Chiniofon

Synonym. Pulvis Chiniofoni.

Chiniofon is a mixture of approximately four parts by weight of 7-iodo-8-hydroxyquinoline-5-sulphonic acid and one part by weight of Sodium Bicarbonate. It contains not less than 28·2 per cent., and not more than 29·6 per cent., of I, and not less than 18 per cent., and not more than 22 per cent., of $NaHCO_3$.

Characters. A light yellow powder; odourless; taste, bitter with a sweetish after-taste.

Soluble, with effervescence, in about 25 parts of *water*; insoluble in *alcohol* (*95 per cent.*), in *ether*, and in *chloroform*.

Tests for Identity. Decomposes when heated at about 275°.

When *dilute hydrochloric acid* is added to a saturated aqueous solution, the colour changes from deep orange to pale yellow, and a yellow crystalline precipitate is slowly produced.

To 10 millilitres of a 1 per cent. w/v aqueous solution add 5 drops of *test-solution of ferric chloride*; a deep olive-green colour is produced.

To 10 millilitres of a 1 per cent. w/v aqueous solution add 5 millilitres of *solution of copper sulphate*; a dense white precipitate is produced.

Make 5 millilitres of a 1 per cent. w/v aqueous solution slightly acid with *dilute hydrochloric acid*, add 5 millilitres of *chloroform* and one drop of a 10 per cent. w/v aqueous solution of *sodium nitrite*, and shake; the chloroform is coloured violet.

Test for Purity. Make 5 millilitres of a 1 per cent. aqueous solution slightly acid with *dilute hydrochloric acid*, and shake with 5 millilitres of *chloroform*; no violet colour appears in the chloroform (absence of free iodine).

Assay. *For iodine.* Mix about 0·2 gramme, accurately weighed, with about 1 gramme of *anhydrous sodium carbonate* in a nickel crucible 20 millimetres in diameter, moisten with *water*, and dry at 100°. Fill the crucible completely with *anhydrous sodium carbonate* well pressed down; invert the crucible and contents into a nickel crucible, 25 millimetres in diameter, containing a layer of *anhydrous sodium carbonate*, and add more *anhydrous sodium carbonate* to seal the junction of the two crucibles. Heat for fifteen minutes over a Bunsen flame in such a manner that the outer crucible is a uniform dull red; allow to cool, and dissolve the residue in 100 millilitres of hot *water*; filter, and wash the filter with *water* until the washings are neutral to *litmus*. Allow the solution to cool, and add sufficient *water* to produce about 500 millilitres. Neutralise the solution with *sulphuric acid* (*50 per cent. v/v*), using *solution of methyl orange* as indicator. Add 1 millilitre *sulphuric acid* (*50 per cent. v/v*), 0·2 millilitre of *bromine* and a small piece (about 0·05 gramme) of *marble*, and boil briskly for ten minutes. Allow to cool, add 0·2 millilitre of a 25 per cent. w/v solution of *phenol* in *glacial acetic acid*, and allow to stand for at least two minutes. Add 2 grammes of *potassium iodide*, and titrate with *N/10 sodium thiosulphate*, using *mucilage of starch* as indicator. Each millilitre of *N/10 sodium thiosulphate* is equivalent to 0·002116 gramme of I.

For sodium bicarbonate. Place about 0·5 gramme, accurately

weighed, in a dry test-tube 150 millimetres in length and 20 millimetres in diameter, and insert a loose plug of glass wool about half way down the tube. Place the test-tube in a 750-millilitre filtering flask, containing 50 millilitres of *N/10 barium hydroxide*. Close the neck of the flask with a stopper, through which passes the tube of a 50 millilitre separating funnel, in such a manner that the tube of the separating funnel enters the test-tube. Exhaust the flask rapidly until a pressure of 20 millimetres of mercury is obtained, and close the exit tube. Through the separating funnel add gradually 10 millilitres of freshly boiled and cooled *water*; when effervescence has ceased, add about 1 millilitre of *dilute hydrochloric acid*, followed by two quantities of 5 millilitres of freshly boiled and cooled *water*. Allow to stand for at least twelve hours, and titrate the excess of *N/10 barium hydroxide* with *N/10 oxalic acid*, using *solution of phenolphthalein* as indicator. Each millilitre of *N/10 barium hydroxide* is equivalent to 0·0042 gramme of $NaHCO_3$.

NOTE.—Solutions of Chiniofon are decomposed by boiling.

DOSES

Metric.	Imperial.
0·06 to 0·5 gramme.	1 to 8 grains.
By rectal injection.	
1 to 5 grammes.	15 to 75 grains.

CINCHOPHENUM
Cinchophen

Page 123,

delete line 22;

insert

"0·3 to 0·6 gramme.	5 to 10 grains.".

DIGITALIS PULVERATA
Powdered Digitalis

Page 144, line 9,

delete "*No. 20 powder*";

insert "powder not more coarse than a *moderately coarse powder*".

line 12,

delete "0·1";

insert "0·08".

ERGOMETRINA

[Ergomet.]

Ergometrine

$C_{19}H_{23}O_2N_3$ . . . . Mol. Wt. 325·2

Ergometrine is an alkaloid, obtained from ergot and purified by crystallisation from a suitable organic solvent. It occurs in two forms which are differentiated by their melting-points. The crystals may contain a variable proportion of solvent of crystallisation.

Characters. Colourless crystals, which become coloured on exposure to air or light; odourless; taste, slightly bitter.

Slightly soluble in *water*, producing a solution which shows a blue fluorescence; moderately soluble in *dehydrated alcohol*; sparingly soluble in *chloroform*; moderately soluble in *acetone*; sparingly soluble in *benzene*.

Tests for Identity. Dissolve 0·001 gramme in 5 millilitres of *water*; add slowly to 1 millilitre of the solution 2 millilitres of *solution of dimethylaminobenzaldehyde*, and mix; a deep blue colour is produced.

Dissolve 0·001 gramme in 1 millilitre of *glacial acetic acid*, containing a trace of *ferric chloride*, and add 2 drops of *sulphuric acid*; a purplish blue colour is produced.

Tests for Purity. *Melting-point* of the lower-melting form, determined on the air-dried substance, the rate of rise of temperature being 4° per minute, 162° to 164°, with decomposition; *melting-point* of the higher-melting form, determined on material which has been dried at 140° in vacuo for one hour, 212° with decomposition; *specific rotation* in a 1·5 per cent. w/v solution in *dehydrated alcohol*, determined on the air-dried substance and calculated with reference to the substance from which the associated solvent has been removed (sodium light), + 40° to + 43°, (mercury light), + 60° to + 63°. The proportion of associated solvent is determined by heating at 140° in vacuo for one hour.

DOSES

Metric.	Imperial.
0·0005 to 0·001 gramme.	1/120 to 1/60 grain.
By intramuscular injection.	
0·00025 to 0·0005 gramme.	1/240 to 1/120 grain.
By intravenous injection.	
0·000125 to 0·00025 gramme.	1/480 to 1/240 grain.

ERGOTA

Ergot

Page 151,

delete lines 37–45, and

Page 152,

delete line 1;

insert " volume. Mix 1 millilitre with 2 millilitres of *solution of dimethylaminobenzaldehyde*, and allow to stand for five minutes. Mix 1 millilitre of *solution of ergotoxine ethanesulphonate* with 2 millilitres of *solution of dimethylaminobenzaldehyde*, and allow to stand for five minutes. Determine the ratio of the ".

ERGOTOXINÆ ÆTHANOSULPHONAS

Ergotoxine Ethanesulphonate

Page 153, line 21,

delete " cool," and " on exposure to light,".

line 28,

delete " + 112° ";
insert " + 119° ".

EXTRACTUM BELLADONNÆ LIQUIDUM

Liquid Extract of Belladonna

Page 157, line 20,

delete "63 to 73";
insert "48 to 66".

EXTRACTUM ERGOTÆ LIQUIDUM

Liquid Extract of Ergot

Page 165,

after line 10,

insert " *CAUTION—In any part of the British Empire*

in which Liquid Extract of Ergot is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See page 12.*)".

EXTRACTUM HYOSCYAMI LIQUIDUM

Liquid Extract of Hyoscyamus

Page 173, line 38,

delete "60 to 70";

insert "50 to 60".

EXTRACTUM PITUITARII LIQUIDUM

Pituitary (Posterior Lobe) Extract

Page 182,

delete lines 40–44, and

Page 183,

delete lines 1–9;

insert "**Containers.** The containers of Pituitary (Posterior Lobe) Extract are either sealed glass ampoules or glass phials, sealed so as to allow the withdrawal of successive doses on different occasions. If containers of the latter form are used, Pituitary (Posterior Lobe) Extract contains a sufficient proportion of some antiseptic to prevent the growth of any organism, which may be accidentally introduced in the process of removing a portion of the contents of the container. The glass ampoules, or glass phials, comply with the *tests for limit of alkalinity of glass*.

Storage. Pituitary (Posterior Lobe) Extract should be kept at as low a temperature as possible above its freezing-point. Under these conditions the product may be expected to retain its potency for at least eighteen months after the date of manufacture, provided that the reaction lies between the limits of *p*H 3 and *p*H 4.

Labelling. The label on each container states the number of Units per millilitre.

The label on the container, or the label or wrapper on the package, states:—(1) the date of manufacture; (2) the date after which the preparation is not intended to be used.".

EXTRACTUM SENEGÆ LIQUIDUM

Liquid Extract of Senega

Page 183, line 30,
delete "44 to 54";
insert "38 to 44".

EXTRACTUM STRAMONII LIQUIDUM

[Ext. Stramon. Liq.]

Liquid Extract of Stramonium

Liquid Extract of Stramonium contains 0·25 per cent. w/v of the alkaloids of Stramonium, calculated as hyoscyamine (limits, 0·225 to 0·275).

Stramonium, in *moderately coarse powder* . .	1000 grammes
Alcohol (45 per cent.) .	a sufficient quantity

Exhaust the Stramonium by percolation with Alcohol (45 per cent.), reserving the first 850 millilitres of the percolate. Remove the alcohol from the remainder of the percolate by distillation under reduced pressure at a temperature not exceeding 60°; evaporate the residue to a soft extract at a temperature not exceeding 60°; dissolve this in the reserved portion. Determine the proportion of alkaloids in the liquid, thus obtained, by the Assay described below. To the remainder of the liquid add sufficient Alcohol (45 per cent.) to produce a Liquid Extract of Stramonium of the required strength. Set aside for not less than twenty-four hours; filter, if necessary.

Assay. To 20 millilitres in a separator add 10 millilitres of *water* and 2 millilitres of *dilute solution of ammonia*, and complete the Assay as directed under 'Tinctura Belladonnæ', commencing with the words "and shake with successive portions of *chloroform*. . .".

Alcohol content (determined by *Method I*), 28 to 40 per cent. v/v of ethyl alcohol.

Preparation. Tinctura Stramonii.

DOSES

Metric.	Imperial.
0·03 to 0·2 mil.	$^1/_2$ to 3 minims.

Liquid Extract of Stramonium contains in 0·2 mil 0·0005 gramme, and in 3 minims about $^1/_{120}$ grain, of the alkaloids of Stramonium, calculated as hyoscyamine.

EXTRACTUM STRAMONII SICCUM

[Ext. Stramon. Sicc.]

Dry Extract of Stramonium

Dry Extract of Stramonium contains 1 per cent. of the alkaloids of Stramonium, calculated as hyoscyamine (limits, 0·9 to 1·1).

Stramonium, in *moderately coarse powder*	1000 grammes
Alcohol (95 per cent.)	of each a sufficient quantity
Starch	

Percolate the Stramonium with Alcohol (95 per cent.) until 4000 millilitres of percolate have been obtained. Determine the proportion of total solids in the percolate by evaporating 20 millilitres, drying the residue at 80°, and weighing. Determine also the proportion of alkaloids in the percolate by the assay described below. Having thus determined the proportion of total solids and of alkaloids in the percolate, calculate the amount of each that the remainder of the percolate will yield. Calculate the amount of Starch that must be added to the percolate to produce a dry extract containing 1 per cent. of alkaloids. Add to the percolate a somewhat smaller amount of Starch than calculation has shown to be necessary; remove the alcohol, evaporate to dryness under reduced pressure at a temperature not exceeding 60°, and dry finally in a current of air at 80°. Powder the residue, add the final necessary amount of Starch and triturate in a mortar until thoroughly mixed. Pass the powdered Extract through a No. 22 sieve.

In making Dry Extract of Stramonium the Alcohol (95 per cent.) may be replaced by Industrial Methylated Spirit, diluted so as to be of equivalent alcoholic strength, provided that the law and the statutory regulations governing the use of Industrial Methylated Spirit are observed.

Assay. Carry out the Assay as directed under "Extractum Belladonnæ Siccum". Each millilitre of *N/50 sulphuric acid* is equivalent to 0·005784 gramme of hyoscyamine.

Storage. Dry Extract of Stramonium should be kept in a small, wide-mouthed, well-closed container, and stored in a cool place.

DOSES

Metric.	Imperial.
0·015 to 0·06 gramme.	1/4 to 1 grain.
In post-encephalitic and similar conditions.	
0·06 to 0·5 gramme.	1 to 8 grains.

Dry Extract of Stramonium contains in 0·06 gramme 0·0006 gramme, and in 8 grains about 8/100 grain, of the alkaloids of Stramonium, calculated as hyoscyamine.

FERRI ET AMMONII CITRAS

Iron and Ammonium Citrate

Page 186,

delete line 38;

insert "**1·3 to 2·6 grammes. 20 to 40 grains.**".

delete lines 39 and 40;

insert "Iron and Ammonium Citrate contains in 2·6 grammes about 0·5 gramme, and in 40 grains about 8 grains, of iron.".

FERRI SUBCHLORIDUM CITRATUM

[Ferr. Subchlorid. Cit.]

Citrated Ferrous Chloride

Citrated Ferrous Chloride is a preparation of ferrous chloride and citric acid. It may be prepared by the following method:—heat a mixture of equal volumes of Hydrochloric

Acid and Distilled Water with an excess of Iron, until the reaction ceases; determine the proportion of ferrous chloride in the solution by the Assay described below; dissolve in the solution a quantity of Citric Acid equal in weight to one-tenth of the ferrous chloride present; filter the solution, evaporate to the consistence of a thick paste, and dry at 80°. It contains not less than 68 per cent. of ferrous iron, calculated as $FeCl_2$, and not more than 5·8 per cent. of ferric iron, calculated as $FeCl_3$.

Characters. A buff-coloured powder; taste, acid, metallic and astringent.

Almost completely soluble in 1 part of *water*; readily soluble in dilute mineral acids.

Tests for Identity. Yields the *reactions* characteristic of ferrous salts, of chlorides, and of citrates.

Tests for Purity. 0·5 gramme, dissolved in 3 millilitres of *dilute hydrochloric acid*, complies with the *limit test for sulphates*.

Arsenic limit, 10 parts per million.

Assay. *For ferrous iron.* Dissolve about 0·5 gramme, accurately weighed, in 20 millilitres of *dilute sulphuric acid*, and titrate with *N/10 potassium dichromate*, using *solution of potassium ferricyanide* as indicator. Each millilitre of *N/10 potassium dichromate* is equivalent to 0·01268 gramme of $FeCl_2$.

For ferric iron. Dissolve about 1 gramme, accurately weighed, in 20 millilitres of *water* in a stoppered vessel, and add 15 millilitres of *hydrochloric acid* and 2 grammes of *potassium iodide*. Allow to stand for three minutes, and titrate with *N/10 sodium thiosulphate*. Each millilitre of *N/10 sodium thiosulphate* is equivalent to 0·01622 gramme of $FeCl_2$.

Storage. Citrated Ferrous Chloride should be kept in a well-closed container, protected from light.

DOSES

Metric.	Imperial.
0·2 to 0·3 gramme.	3 to 5 grains.

Citrated Ferrous Chloride contains in 0·3 gramme about 0·1 gramme and in 5 grains about 1½ grains, of iron.

FERRUM

Iron

Page 190, lines 6 and 7,

delete "(No. 42 Standard Wire Gauge)".

HISTAMINÆ PHOSPHAS ACIDUS

[Histam. Phosph. Acid.]

Histamine Acid Phosphate

Synonym. Histaminæ Phosphas.

$C_5H_9N_3,2H_3PO_4$ . . . . Mol. Wt. 307·2

Histamine Acid Phosphate is the di-acid phosphate of an organic base, histamine, 4-β-aminoethylglyoxaline. It may be prepared by the action of phosphoric acid on histamine, which may be obtained from natural sources or by synthesis.

Characters. Colourless crystals; odourless.

Soluble in 4·5 parts of *water*; slightly soluble in *alcohol (90 per cent.)*.

Tests for Identity. An aqueous solution is acid to *litmus*.

Dissolve 0·1 gramme in 7 millilitres of *water*, and add 3 millilitres of *solution of sodium hydroxide*; dissolve 0·05 gramme of *sulphanilic acid* in 10 millilitres of *water* containing 2 drops of *hydrochloric acid*, and add 2 drops of a 10 per cent. w/v solution of *sodium nitrite*. Mix the two solutions; a deep red colour is produced.

Dissolve 0·05 gramme in 5 millilitres of hot *water*, and add 10 millilitres of a hot 0·5 per cent. w/v solution of *picrolonic acid* in *alcohol (25 per cent.)*. The crystalline picrolonate deposited on cooling, after washing with *water* and drying at 100°, has a *melting-point* of 266° to 267°.

Yields the *reactions* characteristic of phosphates.

Tests for Purity. *Melting-point* 130° to 133°, after sintering at 127°.

Dissolve 0·1 gramme in 2 millilitres of *sulphuric acid*; the solution is colourless (limit of readily carbonisable impurities).

0·2 gramme loses, when dried in a vacuum desiccator, not more than 0·002 gramme.

Sterilisation of a Solution. A solution of Histamine Acid Phosphate for injection is sterilised by *heating in an autoclave*, by *Tyndallisation*, or by *filtration*. The containers comply with the *tests for limit of alkalinity of glass*.

DOSES

Metric.	Imperial.
By subcutaneous injection:	
0·0005 to 0·001 gramme.	**1/120 to 1/60 grain.**

HYDRARGYRI OXYCYANIDUM

Mercuric Oxycyanide

Page 205,

delete line 41;

insert "Almost completely soluble in about 18 parts of *water*.".

Page 206, line 6,

after "**Tests for Purity**",

insert "1 gramme, dissolved in 200 millilitres of *water*, gives a clear solution.".

HYDRARGYRUM CUM CRETA

Mercury with Chalk

Page 210, line 31,

after "cool, dilute with 25 millilitres of *water*,",

insert "add sufficient *solution of potassium permanganate* to produce a permanent pink colour. Decolourise by the addition of a trace of *ferrous sulphate*,".

HYOSCYAMUS

Hyoscyamus

Page 213, line 32,

delete "80";

insert "30".

line 34,

delete "20";

insert "15".

delete "3";

insert "4".

lines 37–39,

delete "Mix the acid liquids, neutralise with *dilute solution of ammonia*, using *litmus* as indicator, and evaporate in vacuo to about 50 millilitres at a temperature not exceeding 40°.".

Page 214, line 4,
before "shake",
insert "without delay".

line 5,
after "effected,",
insert "carrying out the extraction as rapidly as possible and ".

INDICARMINUM
Indigo Carmine

Page 216,
after line 40,
insert "**Sterilisation of a Solution.** A solution of Indigo Carmine for injection is sterilised by *heating in an autoclave*, or by *Tyndallisation*.".

INFUSUM DIGITALIS RECENS
Fresh Infusion of Digitalis

Page 221, line 23,
delete "5";
insert "4".

INJECTIO BISMUTHI
Injection of Bismuth

Page 226, lines 35 and 36,
delete "Distilled Water, freshly redistilled from glass apparatus,";
insert "Sterilised Water,".

Page 227,
delete lines 1–9;
insert "Dissolve the Dextrose and the Cresol in 50 millilitres of Sterilised Water, triturate the Precipitated Bismuth with the solution, and add sufficient Sterilised Water to produce the required volume. Mix thoroughly, transfer to suitable sterilised containers, in which are glass balls, and sterilise by *heating in an autoclave*, or by *Tyndallisation*.".

INJECTIO BISMUTHI OXYCHLORIDI

[Inj. Bism. Oxychlor.]

Injection of Bismuth Oxychloride

Bismuth Oxychloride, in *very fine powder*	10	grammes
Dextrose	5	grammes
Cresol	0·5	millilitre
Sterilised Water, sufficient to produce	100	millilitres

Dissolve the Dextrose and the Cresol in 50 millilitres of Sterilised Water, triturate the Bismuth Oxychloride with the solution, and add sufficient Sterilised Water to produce the required volume. Mix thoroughly, transfer to suitable sterilised containers, and sterilise by *Tyndallisation*.

DOSES

Metric.	Imperial.
By intramuscular injection.	
1 to 2 mils.	**15 to 30 minims.**

Injection of Bismuth Oxychloride contains in 2 mils 0·2 gramme, and in 30 minims about 3 grains, of Bismuth Oxychloride.

INJECTIO BISMUTHI SALICYLATIS

Injection of Bismuth Salicylate

Page 227, line 27,

after " solution ",

insert " in a sterilised mortar ".

line 29,

after " containers,",

insert " seal,".

INJECTIO MERSALYLI

[Inj. Mersalyl.]

Injection of Mersalyl

Mersalyl	10	grammes
Theophylline	5	grammes
Sodium Hydroxide	0·05	gramme
	or a sufficient quantity	
Sterilised Water, sufficient to produce	100	millilitres

Add the Mersalyl to about 80 millilitres of Sterilised Water. When solution has been effected, add the Theophylline, and stir until dissolved, without the aid of heat. Dissolve the Sodium Hydroxide in about 2 millilitres of Sterilised Water and add sufficient of the solution to the solution of Mersalyl and Theophylline, until 1 drop of the resulting solution gives a green colour with 1 drop of *solution of bromothymol blue*, and a full yellow colour with 1 drop of *solution of thymol blue*. Then add sufficient Sterilised Water to produce the required volume. Mix thoroughly, clarify the solution by filtration through a filter candle, transfer to suitable sterilised containers, and sterilise by heating in an autoclave for twenty minutes at 110°, or by *Tyndallisation*.

Storage.—Injection of Mersalyl should be protected from light.

DOSES

Metric.	Imperial.
0·5 to 2 mils.	8 to 30 minims.

Injection of Mersalyl contains in 2 mils about 0·2 gramme of Mersalyl, and about 0·1 gramme of Theophylline; and in 30 minims about 3 grains of Mersalyl, and about 1½ grains of Theophylline.

INJECTIO SODII CHLORIDI ET ACACIÆ

Injection of Sodium Chloride and Acacia

Page 230, line 29,

delete "Distilled Water, freshly prepared";
insert "Sterilised Water".

Page 230, line 31,

delete " Distilled " ;

insert " Sterilised ".

line 33,

delete " Distilled " ;

insert " Sterilised ".

Page 231,

delete lines 5–9 ;

insert " paper and linen, and transfer to glass containers. Close the containers so as to exclude bacteria, and sterilise by *heating in an autoclave.*".

INSULINUM

Insulin

Page 231, line 24,

after " 60 per cent. v/v ",

insert " , together with a sufficient quantity of Hydrochloric Acid to make the *reaction* of the mixture not less than *p*H 3·0 and not more than *p*H 3·5 ".

Page 232,

delete lines 11–16 ;

insert " between limits corresponding to the values *p*H 3 and *p*H 4. To the acidulated water, used for dissolving the powder, it is usual to add a sufficient proportion of some antiseptic to prevent the growth of any organism, which may be accidentally introduced in the process of removing a portion of the contents of the container. The solution is sterilised.".

delete lines 19 and 20.

lines 31–37,

delete "The label on each container states the number of Units per millilitre, and the date of manufacture." and the paragraph on "**Storage**";

insert "**Storage.** Insulin in solution should be kept at as low a temperature as possible above its freezing-point, and should

not be exposed to temperatures exceeding 20°. Under these conditions the product may be expected to retain its potency for at least eighteen months after the date of manufacture, provided that the reaction lies between the limits of *p*H 3 and *p*H 4.

Labelling. The label on each container states the number of Units per millilitre.

The label on the container, or the label or wrapper on the package, states:—(1) the date of manufacture; (2) the date after which the preparation is not intended to be used.".

Page 233,

delete lines 17 and 18;

insert " When Insulin is prescribed, Insulin in solution, containing 20 Units per millilitre, shall be dispensed, unless a solution of some other strength, or Insulin in tablet form, is specified.".

IODOFORMUM

Iodoform

Page 233, line 32,

delete " sparingly soluble in *benzene* ";

insert " soluble in 7·5 parts of *benzene* ".

IPECACUANHA

Ipecacuanha

Page 237, line 25,

after " shake well ",

insert " and frequently during fifteen minutes ".

LACTOSUM

Lactose

Page 243,

delete lines 18–21;

insert " Shake 5 grammes with 20 millilitres of *alcohol (90 per cent.)* for ten minutes, and filter; 10 millilitres of the filtrate, evaporated to dryness, leaves not more than 0·005 gramme of residue (limit of more soluble sugars).".

LINIMENTUM BELLADONNÆ

Liniment of Belladonna

Page 248, line 9,

delete "70 to 75";

insert "60 to 70".

LIQUOR ADRENALINÆ HYDROCHLORIDI

Solution of Adrenaline Hydrochloride

Page 251,

after line 17,

insert "*CAUTION.—In any part of the British Empire in which Solution of Adrenaline Hydrochloride* (*Epinephrine Hydrochloride Solution*) *is controlled by law, care must be taken that the provisions of such law are duly complied with.* (*See Page 12.*)".

line 19, to the "*Synonyms*"

add "Epinephrine Hydrochloride Solution.".

LIQUOR CALCIFEROLIS

[Liq. Calciferol.]

Solution of Calciferol

Solution of Calciferol is a solution of calciferol in oil. It contains in 1 gramme 3000 *Units of antirachitic activity* (*vitamin D*).

Solution of Calciferol may be prepared by warming to 40° a 1 per cent. suspension of Calciferol in a suitable vegetable oil, such as Arachis Oil, Carbon Dioxide being bubbled through it in order to facilitate solution, and by adding a sufficient quantity of the oil to produce a solution of the required strength.

Assay. Determine the antirachitic activity in relation to the Standard Preparation of antirachitic vitamin (vitamin D) by

the *biological assay of antirachitic vitamin* (*vitamin D*), and express the result in Units per gramme.

Storage. Solution of Calciferol should be kept in a well-closed container, protected from light, and stored in a cool place.

Labelling. The label on the container states the number of *Units of antirachitic activity* (*vitamin D*) in 1 gramme.

DOSES

Metric.	Imperial.
Prophylactic (daily) for an infant	
0·3 to 0·6 mil. (1000 to 2000 Units).	5 to 10 minims.
Therapeutic (daily) for an infant	
0·6 to 1 mil. (2000 to 3000 Units).	10 to 15 minims.

Solution of Calciferol contains in 1 mil about 3000 Units, and in 15 minims about 3000 Units, of antirachitic activity.

LIQUOR CRESOLIS SAPONATUS

Solution of Cresol with Soap

Page 258,

delete lines 23 and 24;

insert "Miscible in all proportions, up to 10 per cent. v/v, with *water*, and in all proportions with *alcohol* (*95 per cent.*)".

LIQUOR ERGOSTEROLIS IRRADIATI

Solution of Irradiated Ergosterol

Pages 259 and 260,

delete this monograph.

LIQUOR FERRI PERCHLORIDI

Solution of Ferric Chloride

Page 261, line 6,

after "*water*;",

insert "add 5 grammes of *ammonium chloride*,".

LIQUOR IODI AQUOSUS

[Liq. Iod. Aquos.]

Aqueous Solution of Iodine

Synonyms. Lugol's Solution: Liquor Iodi Compositus.

Aqueous Solution of Iodine contains 5 per cent. w/v of Iodine (limits, 4·9 to 5·1), and 10 per cent. w/v of Potassium Iodide (limits, 9·8 to 10·2).

Iodine	50 grammes
Potassium Iodide . . .	100 grammes
Distilled Water, sufficient to produce	1000 millilitres

Dissolve the Potassium Iodide and the Iodine in 100 millilitres of Distilled Water; add sufficient Distilled Water to produce the required volume.

Assay. Dilute 25 millilitres with *water* to 100 millilitres.

For iodine. To 20 millilitres of the diluted solution add 10 millilitres of *water*, and titrate with *N/10 sodium thiosulphate*. Each millilitre of *N/10 sodium thiosulphate* is equivalent to 0·01269 gramme of I.

For potassium iodide. To 10 millilitres of the diluted solution add 20 millilitres of *water* and 40 millilitres of *hydrochloric acid*, and titrate with *M/20 potassium iodate*, shaking vigorously until the dark brown solution becomes only light brown in colour; add 5 millilitres of *chloroform*, and continue the titration until the chloroform becomes colourless and the supernatant liquid is clear yellow. From the quantity of *M/20 potassium iodate* required, subtract one quarter of the quantity of *N/10 sodium thiosulphate* required in the assay for iodine. Each millilitre of *M/20 potassium iodate* is equivalent to 0·0166 gramme of KI.

Storage. Aqueous Solution of Iodine should be kept in a well-closed, glass stoppered bottle.

DOSES

Metric.	Imperial.
0·3 to 1 mil.	5 to 15 minims.

Aqueous Solution of Iodine contains in 1 mil 0·05 gramme of Iodine and about 0·13 gramme of total iodine, free and combined; and in 15 minims about $^4/_5$ grain of Iodine, and about 2 grains of total iodine, free and combined.

LIQUOR IODI SIMPLEX

Simple Solution of Iodine

Page 266, last line,

delete "0·0005";
insert "0·002".

LIQUOR SODII CHLORIDI PHYSIOLOGICUS

Physiological Solution of Sodium Chloride

Pages 273 and 274,

delete this monograph;
insert

LIQUOR SODII CHLORIDI PHYSIOLOGICUS

[Liq. Sod. Chlorid. Physiol.]

Physiological Solution of Sodium Chloride

Synonyms. Physiological Saline Solution: Normal Saline Solution.

Sodium Chloride . . .	9 grammes
Distilled Water, sufficient to produce	1000 millilitres

Dissolve; filter; sterilise by *heating in an autoclave*, or by *Tyndallisation*, or by *filtration*.

Physiological Solution of Sodium Chloride for Injections. Physiological Solution of Sodium Chloride, if it is intended for injection, is prepared with Sterilised Water.

Physiological Solution of Sodium Chloride for Injections, kept in a container which is closed with cotton-wool, is used within one month after its preparation. If kept in a container which is sealed by fusion of the glass, or by some equally effective method, it may be stored for a longer period.

MENTHOL

Menthol

Page 281, line 34,
after "*Mentha*",
insert ", or prepared synthetically".

Page 282, line 1,
delete "43°";
insert "44°".

line 2,
delete "lævo-rotatory, and";
after "*litmus.*",
insert "*Specific rotation*, in a 10 per cent. solution in *alcohol* (*90 per cent.*), − 49° to − 50°".

MERSALYLUM

[Mersal.]

Mersalyl

$(HgOH)CH_2{\cdot}CH(OCH_3)CH_2{\cdot}NHCO{\cdot}C_6H_4{\cdot}O{\cdot}CH_2{\cdot}COONa$

Mol. Wt. 505·7

Mersalyl is the sodium salt of salicyl-(γ-hydroxymercuri-β-methoxypropyl)-amide-O-acetic acid. It may be prepared by the action of mercuric acetate and methyl alcohol on salicylallylamide-O-acetic acid, and subsequent conversion to the sodium salt. It contains not less than 2·5 per cent., and not more than 2·8 per cent., of N, and not less than 38·5 per cent., and not more than 40·5 per cent., of Hg, both calculated with reference to the substance dried in a vacuum desiccator.

Characters. A white powder; odourless; taste, bitter. Deliquescent.

Soluble in about 1 part of *water*, and in about 3 parts of *alcohol* (*95 per cent.*); insoluble in *ether*, and in *chloroform*; soluble in about 2 parts of *methyl alcohol*.

Tests for Identity. Dissolve 0·5 gramme in 1 millilitre of *water*, add 1 millilitre of *formic acid*, and boil under a reflux condenser for fifteen minutes. Decant while hot, allow the liquid to

cool, and collect the crystals of salicylallylamide-O-acetic acid; *melting-point* of the crystals, after washing several times with *water* and drying in a vacuum desiccator, 119° to 121°.

Dissolve 0·2 gramme in 15 millilitres of *water*, add 5 millilitres of *hydrochloric acid*, and distil 5 millilitres; the distillate, when tested for methyl alcohol as described under 'Alcohol', gives a deep violet colour.

Tests for Purity. Dissolve 0·5 gramme in 10 millilitres of *water*, and add 2 drops of *solution of sodium sulphide*; no colour is produced (limit of mercuric salts and heavy metals).

Dissolve 0·1 gramme in 5 millilitres of water, add 2 drops of *nitric acid*, filter, and add 2 drops of *solution of silver nitrate*; no immediate opalescence is produced (limit of chloride).

Dissolve 0·1 gramme in 5 millilitres of *water*, add 2 drops of *hydrochloric acid*, filter, and add 2 drops of *solution of barium chloride*; no immediate turbidity is produced (limit of sulphate).

Dissolve 0·5 gramme in 10 millilitres of *water*, add 1 millilitre of *dilute sulphuric acid*, filter, and add 0·05 millilitre of *N/10 potassium permanganate*; no immediate decolorisation is produced (limit of foreign organic matter).

Arsenic limit, 10 parts per million.

Loses, when dried in a vacuum desiccator, not more than 7 per cent. of its weight.

Assay. *For nitrogen.* Heat in a long-necked flask about 0·4 gramme, accurately weighed, with 1 gramme of *potassium sulphate* and 5 millilitres of *nitrogen-free sulphuric acid* until a clear colourless liquid is obtained. Cool, dilute with *water*, transfer to an ammonia distillation apparatus, add 1 gramme of *sodium thiosulphate*, dissolved in 50 millilitres of *solution of sodium hydroxide*, and distil the liberated ammonia into 50 millilitres of *N/50 sulphuric acid*; titrate the excess of acid with *N/50 sodium hydroxide*, using *solution of methyl red* as indicator. Each millilitre of *N/50 sulphuric acid* is equivalent to 0·00028 gramme of N.

For mercury. Dissolve about 0·5 gramme, accurately weighed, in 100 millilitres of *water*, add 15 millilitres of *hydrochloric acid*, boil under a reflux condenser for three hours, add 200 millilitres of hot *water*, and pass in *hydrogen sulphide* for fifteen minutes. Filter while hot through a Gooch crucible, wash the precipitate first with *solution of hydrogen sulphide*, then with *alcohol (95 per cent.)* and finally with *carbon disulphide*, dry at 110°, and weigh. Each gramme of precipitate is equivalent to 0·8622 gramme of Hg.

Storage. Mersalyl should be kept in a well-closed container.

Preparation. Injection of Mersalyl.

Solutions of Mersalyl, containing sodium chloride or other salt, may become toxic unless some substance, such as theophylline, which in-

hibits the decomposition of the mercurial complex, is present. For injections, Injection of Mersalyl should be used.

METHYLIS SALICYLAS

Methyl Salicylate

Page 282, line 33,

after "*volatile oils*",

insert ", omitting the preliminary neutralisation of the free acid with *N/10 aqueous potassium hydroxide*, boiling for one and a half hours, and deducting, from the difference between the titrations, the volume of *N/2 alcoholic potassium hydroxide* equivalent to the volume of *N/10 sodium hydroxide* required in the test for limit of free acid".

NEOARSPHENAMINA

Neoarsphenamine

Page 292,

delete line 7;

insert ", and the solution is used immediately after preparation.".

OLEUM ABIETIS

Oil of Siberian Fir

Page 297, line 20,

delete "35 per cent. w/w";

insert "33 per cent. w/w".

OLEUM CAJUPUTI

Oil of Cajuput

Page 301, line 8,

delete "60 per cent. w/w";

insert "65 per cent. w/w".

line 14,

delete "1·462";

insert "1·464".

OLEUM CHENOPODII

Oil of Chenopodium

Page 303, line 13,

delete "0·960 to 0·980";
insert "0·962 to 0·983".

OLEUM IODISATUM

[Ol. Iodisat.]

Iodised Oil

Iodised Oil is an iodine addition product of poppy-seed oil, and may be prepared by treating poppy-seed oil with hydriodic acid. It is placed in previously sterilised containers, which are filled as completely as possible, and then sealed so as to exclude bacteria. It contains not less than 39 per cent., and not more than 41 per cent., of combined iodine.

Characters. A colourless or pale yellow, clear, viscous, oily liquid; odour, slightly alliaceous; taste, bland and oily.

On exposure to air and sunlight, it decomposes and develops a dark brown colour.

Insoluble in *water*; soluble in *ether*, in *chloroform*, and in *light petroleum*.

Tests for Identity. *Specific gravity* (15·5°/15·5°), about 1·34.

Boil 1 drop with 2 millilitres of *glacial acetic acid* and 0·1 gramme of *zinc powder* for two minutes; add 5 millilitres of *water*, shake, decant from any undissolved zinc, and add 1 millilitre of *solution of hydrogen peroxide*; iodine is liberated.

Tests for Purity. Shake 1 gramme with 10 millilitres of warm *alcohol* (*95 per cent.*), previously neutralised to *phenolphthalein*, and titrate with *N/10 sodium hydroxide*, using *solution of phenolphthalein* as indicator; not more than 1 millilitre is required (limit of acid).

Dissolve 1 gramme in 10 millilitres of *ether*, and add 1 drop of *solution of ammonium hydrosulphide*; no darkening is produced (absence of mercury).

Dissolve 1 gramme in 20 millilitres of *acetone*, add 1 gramme of *sodium iodide*, and set aside in a stoppered flask in the dark for thirty minutes, shaking occasionally; then add 50 milli-

litres of *water*, and titrate with *N/10 sodium thiosulphate*, using *mucilage of starch* as indicator; not more than 0·5 millilitre is required (limit of chloro-iodine compounds).

Dissolve 1 gramme in 5 millilitres of *chloroform*, add 1 gramme of *potassium iodide* dissolved in 20 millilitres of *water*, shake, and titrate with *N/10 sodium thiosulphate*; not more than 0·1 millilitre is required (limit of free iodine).

Complies with the *tests for sterility*.

Assay. Boil about 1 gramme, accurately weighed, with 10 millilitres of *glacial acetic acid* and 1 gramme of *zinc powder* for one hour under a reflux condenser. Add through the condenser tube 30 millilitres of hot *water*, filter through cotton-wool, wash the flask with two quantities of 20 millilitres of hot *water*, and pass the washings through the filter. Cool the filtrate, add 15 millilitres of *hydrochloric acid* and 5 millilitres of *solution of potassium cyanide*, and titrate with *M/20 potassium iodate* until the dark brown solution, which is formed, becomes light brown; add 5 millilitres of *mucilage of starch*, and continue the titration until the blue colour disappears. Each millilitre of *M/20 potassium iodate* is equivalent to 0·01269 gramme of I.

Storage. Iodised Oil should be kept in a well-filled container, protected from light.

OLEUM LAVANDULÆ

Oil of Lavender

Page 308, line 2,

delete "14 per cent. w/w";

insert "12 per cent. w/w".

OLEUM LIMONIS

Oil of Lemon

Page 308,

after line 30,

insert "5 grammes, when evaporated rapidly in a flat-bottomed dish, 9 cm. in diameter and 1·5 cm. in depth, on a boiling water-bath, leaves not less than 0·1 gramme, and not more than 0·15 gramme, of non-volatile residue.".

OLEUM MENTHÆ PIPERITÆ

Oil of Peppermint

Page 309, line 31,

delete "4·5";
insert "4·0".

line 41,

delete "0·910";
insert "0·915".

line 42,

delete "− 32°";
insert "− 30°".

OLEUM MORRHUÆ

Cod-liver Oil

Page 310,

delete this monograph;
insert

OLEUM MORRHUÆ

[Ol. Morrh.]

Cod-liver Oil

Cod-liver Oil is the oil, obtained from the fresh liver of the cod, *Gadus morrhua* Linn., and other species of *Gadus*, and freed from solid fat by filtration at about 0°. It contains in 1 gramme not less than 600 *Units of vitamin A activity*, and not less than 85 *Units of antirachitic activity* (*vitamin D*).

Characters. A pale yellow liquid; odour, slight, but not rancid; taste, bland or slightly fishy.

Slightly soluble in *alcohol* (*90 per cent.*); miscible with *ether*, with *chloroform*, and with *light petroleum* (*boiling-point, 50° to 60°*).

Tests for Purity. *Specific gravity* (15·5°/15·5°), 0·922 to 0·929; *refractive index* at 40°, 1·4705 to 1·4745; *acid value*, not greater

than 1·2; *saponification value*, 180 to 190; *unsaponifiable matter*, not more than 1·5 per cent.; *iodine value*, 155 to 173.

Remains bright when cooled to 0° and kept at that temperature for three hours.

Assay. *For vitamin A activity.* Determine the vitamin A activity in relation to the Standard Preparation of vitamin A by the *assay of vitamin A*, and express the result in Units per gramme.

For antirachitic activity (*vitamin D*). Determine the antirachitic activity in relation to the Standard Preparation of antirachitic vitamin (vitamin D) by the *biological assay of antirachitic vitamin* (*vitamin D*), and express the result in Units per gramme.

Storage. Cod-liver Oil should be kept in a well-filled, well-closed container, and protected from light.

Preparation. Extractum Malti cum Oleo Morrhuæ.

DOSES

Metric.	Imperial.
Prophylactic	
1 to 2 mils. three times daily.	15 to 30 minims.
Therapeutic	
3 to 6 mils. three times daily.	45 to 90 minims.

OLEUM MYRISTICÆ

Oil of Nutmeg

Page 311,

delete lines 11 and 12;

insert "2 grammes, when evaporated rapidly in a flat-bottomed dish, 9 cm. in diameter and 1·5 cm. in depth, on a boiling water-bath, leaves not more than 0·060 gramme of non-volatile residue.".

OLEUM OLIVÆ

Olive Oil

Page 311,

delete lines 32 and 33;

insert "Complies with the *tests for the absence of cotton-seed oil, and of arachis oil.*

Complies with the *test for the absence of sesame oil*, after shaking together equal volumes of the oil, and of a mixture of 9 parts by volume of *alcohol (90 per cent.)* and 1 part by volume of *strong solution of ammonia*, and heating on a boiling water-bath until free from alcohol and ammonia.".

OLEUM ROSMARINI

Oil of Rosemary

Page 312, line 36,

delete "1·464";
insert "1·466".

OLEUM SANTALI

Oil of Sandal Wood

Page 313, line 23,

delete "1·500";
insert "1·505".

OLEUM TEREBINTHINÆ

Oil of Turpentine

Page 315, line 20,

delete "dry";
insert "previously dried".
delete "add";
insert "containing".

Page 315, lines 22 and 23,

delete "laboratory temperature";
insert "15° to 20°".

OXYGENIUM

Oxygen

Page 319,

delete the last two lines, and

Page 320,

delete lines 1 and 2;

insert "Complies with the test for limit of acidity and alkalinity described under 'Nitrogenii Monoxidum'.".

PARAFFINUM LIQUIDUM

Liquid Paraffin

Page 324,

delete lines 16 and 17;

insert "*kinematic viscosity,* not less than 64 centistokes at 37·8°".

delete lines 20–23;

insert "Place 5 millilitres with 5 millilitres of *nitrogen-free sulphuric acid* in a test-tube, 120 millimetres in length and 20 millimetres in internal diameter, which is fitted with a glass stopper and is graduated at 5 and 10 millilitres, and which has been carefully cleaned and dried. Insert the stopper, and shake as vigorously as possible, in the longitudinal direction of the tube, for five seconds. Loosen the stopper, place the tube immediately in a boiling water-bath, supporting it so as to prevent contact of the tube with the bottom or side of the bath, and heat for ten minutes. At the end of the second, fourth, sixth and eighth minutes, remove the tube from the bath, and shake as vigorously as possible, in the longitudinal direction of the tube, for five seconds. At the end of ten minutes transfer the liquids to a small dry separator with ungreased tap, allow to stand for ten minutes, and run off the lower layer into a colourless rectangular glass cell of 10 millimetres internal measurement in the direction of observation. Place the cell in a colorimeter, designed for matching the colour of the solution against colour glasses, and compare the colour of the test liquid with the colour given by the combination of the *colour glasses for the sulphuric acid test on liquid paraffin.* The colour of the test liquid is not deeper than the combined colour of the prescribed glasses, neither with respect to the red component nor with respect to the yellow component.".

PHENOL LIQUEFACTUM

Liquefied Phenol

Page 333, line 32,

after "light.",

insert "Liquefied Phenol may congeal or deposit crystals, if stored below 4°. It should be completely melted before use.".

PHENOLPHTHALEINUM

Phenolphthalein

Page 334, line 15,

delete "254° to 258°";

insert "not below 258°".

PLUMBI ACETAS

Lead Acetate

Page 342, line 3,

delete "1";

insert "2".

POTASSII BICARBONAS

Potassium Bicarbonate

Page 348, line 14,

after "grammes",

insert ", dissolved in 20 millilitres of *dilute nitric acid FeT.*,".

POTASSII CARBONAS

Potassium Carbonate

Page 350, line 11,

after "gramme",

insert ", dissolved in 10 millilitres of *dilute nitric acid FeT.*,".

POTASSII CITRAS

Potassium Citrate

Page 351,

delete lines 33–36;

insert "**Tests for Purity.** 2 grammes, boiled with 25 millilitres of *water* and cooled, requires for neutralisation not more than 0·5 millilitre of either *N/10 sulphuric acid*, or *N/10 sodium hydroxide*, *solution of thymol blue* being used as indicator (limit of alkalinity, or of acidity).".

POTASSII HYDROXIDUM

Potassium Hydroxide

Page 352, line 28,

after "KOH.",

insert "It contains not more than 4 per cent. of K_2CO_3.".

line 32,

delete "Soluble in 0·95 part of *water*, and";

insert "Completely, or almost completely, soluble in 0·95 part of *water*; soluble".

lines 35–39,

delete the test for "limit of carbonate".

Page 353,

delete lines 11–15;

insert "**Assay.** Dissolve about 2 grammes, accurately weighed, in 25 millilitres of *water*, add 5 millilitres of *solution of barium chloride*, and titrate with *N/1 hydrochloric acid*, using *solution of phenolphthalein* as indicator.

To the solution in the flask add *solution of bromophenol blue*, and continue the titration with *N/1 hydrochloric acid*. Each millilitre of *N/1 hydrochloric acid* used in the second titration is equivalent to 0·06910 gramme of K_2CO_3.

Each millilitre of *N/1 hydrochloric acid* used in the combined titrations is equivalent to 0·05611 gramme of total alkali, calculated as KOH.".

PULVIS VITAMINI B_1

[Pulv. Vitamin. B_1]

Adsorbate of Vitamin B_1

Adsorbate of Vitamin B_1 is an adsorbate of the antineuritic vitamin (vitamin B_1) upon *fuller's earth*. It contains in 1 gramme 100 *Units of antineuritic activity* (*vitamin B_1*).

It may be prepared from rice polishings, yeast, wheat embryo, or other suitable materials. The method of preparation from rice polishings is as follows :—The material is extracted with Distilled Water, sufficient Dilute Sulphuric Acid being added to make the *p*H 4·5. Salicylic Acid to a concentration of 0·2 per cent. and *toluene* are then added to prevent bacterial decomposition. The process of extraction is continued for two days, after which the solution is filtered. For each 100 kilograms of the original rice polishings, 3 kilograms of *fuller's earth* is added to the solution, which is then stirred for twenty-four hours. Subsequently, the solution is filtered off, and the powder, after being washed with Distilled Water and Dehydrated Alcohol, is dried. The powder is assayed, and adjusted to contain 100 Units in 1 gramme by thorough mixture with an adsorbate containing more than 100 Units in 1 gramme, or with *fuller's earth*.

Characters. A cream-coloured powder; almost odourless; tasteless.

Insoluble in *water*, and in mineral acids.

Assay. Determine the antineuritic activity in relation to the Standard Preparation of antineuritic vitamin (vitamin B_1) by the *biological assay of antineuritic vitamin* (*vitamin B_1*), and express the result in Units per gramme.

Storage. Adsorbate of Vitamin B_1 should be kept in a well-closed container.

DOSES

Metric.	Imperial.
Prophylactic (daily)	
1 to 2 grammes. (100 to 200 Units).	**15 to 30 grains.**
Therapeutic (daily)	
2 to 6 grammes. (200 to 600 Units).	**30 to 90 grains.**

PYROXYLINUM

Pyroxylin

Page 363, line 3,

delete "*Viscosity*";
insert "*Kinematic viscosity*".

line 4,

delete "3 poises";
insert "370 centistokes".

QUININÆ ET ÆTHYLIS CARBONAS

Quinine Ethyl Carbonate

Page 368, line 15,

delete "95°";
insert "90°".

RHEUM

Rhubarb

Page 374, line 2,

after "dried.",
insert "It is known in commerce as Shensi, Canton, or high-dried rhubarb.".

line 6,

delete "but not shrunken";
insert "not discoloured or lacunose internally".

line 26,

delete "*Ash*, not more than 15 per cent.";
insert "*Acid-insoluble ash*, not more than 1 per cent.".

Page 374,

after line 27,

insert "When examined in screened ultra-violet radiation with a lens, no shining violet points are visible (limit of rhapontic rhubarb).".

SAPO ANIMALIS

Curd Soap

Page 378, line 8,

before "of *N/10 sodium hydroxide*",

insert "not more than 0·4 millilitre".

line 19,

delete "0·025";

insert "0·04".

line 23,

delete "about 20 grammes";

insert "a sufficient quantity".

SAPO DURUS

Hard Soap

Page 379, line 5,

after "acid,",

insert "and".

line 6,

delete "and for limit of free fat,";

after "'Sapo Animalis'",

insert "Carry out the test for limit of free fat, described under 'Sapo Animalis'; the weight of the residue does not exceed 0·05 gramme (limit of free fat).".

lines 14 and 15,

delete "*solidifying-point*, 18° to 23°;".

lines 15 and 16,

after "*acid value*,",

insert "determined on 2 to 3 grammes of the fatty acids,".

SAPO MOLLIS

Soft Soap

Page 380, line 10,

delete "0·2";

insert "0·4".

delete lines 16 and 17;

insert "Carry out the test for limit of free fat, described

under 'Sapo Animalis'; the weight of the residue does not exceed 0·0375 gramme (limit of free fat).".

SERUM ANTIPNEUMOCOCCICUM I

[Serum Antipneumococc. I]

Antipneumococcus Serum (Type I)

CAUTION.—In any part of the British Empire in which Antipneumococcus Serum (Type I) is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

Antipneumococcus Serum (Type I) is serum, or a preparation from serum, containing the immune substances which have a specific therapeutic action, when injected into persons suffering from certain diseases due to *Diplococcus pneumoniæ* (*type I*).

It is prepared by separating the serum from the blood of animals, which have been immunised by graded injections of cultures of *Diplococcus pneumoniæ* (*type I*). The serum may be used in the liquid form, or may be dried. The globulins, containing the specific immune substances, may be obtained from the serum by fractional precipitation, and the precipitate may be used either in solution, or dried. The final sterile product, whether serum, dried serum, solution of globulins, or dried globulins, is distributed in sterilised glass containers, which are sealed so as to exclude bacteria. An antiseptic may be added to the liquid forms.

Characters. The liquid serum is yellow or yellowish-brown. The solution of the globulins is yellowish-brown or greenish-yellow. Both liquid forms are initially transparent, but acquire with age a faint opalescence. They are almost odourless, except for the odour of any antiseptic which may have been added. The solid forms are yellowish-white powders, or yellowish-brown flakes. When dissolved in 10 parts of *water*, they resemble the liquid forms in colour and appearance. The liquid serum does not contain more than 10 per cent. w/v of solid matter. The solution of the globulins does not contain

more than 20 per cent. w/v of solid matter. The solid forms do not contain antiseptic, or other added substance.

Test for Identity. It protects susceptible animals from the lethal action of a virulent culture of *Diplococcus pneumoniæ* (*type I*).

Tests for Purity. All forms comply with the *tests for sterility*. All forms comply with the *tests for freedom from abnormal toxicity*.

Assay. Determine the potency in relation to the Standard Preparation of antipneumococcus serum (type I) by the *biological assay of antipneumococcus serum* (*type I*), and express it in Units per millilitre for liquid preparations, and in Units per gramme for solid preparations.

Storage. Antipneumococcus Serum (type I) should be kept at as low a temperature as possible above its freezing-point.

Labelling. The label or wrapper on the package, or the label on the container, states:—(1) whether the product is serum, dried serum, solution of antitoxic globulins, or dried antitoxic globulins; (2) the date after which the preparation is not intended to be used.

The label on the container states:—(1) the minimum total number of Units in the container; (2) either (*a*) the number of Units in 1 millilitre, or in 1 gramme, or (*b*) the total number of millilitres of liquid, or grammes of dried product, in the container.

Antipneumococcus Serum (type I) should not be used later than two years after the date of manufacture.

DOSES

By intravenous injection.

50,000 to 150,000 Units.

SERUM ANTIPNEUMOCOCCICUM II

[Serum Antipneumococc. II]

Antipneumococcus Serum (Type II)

CAUTION.—In any part of the British Empire in which Antipneumococcus Serum (Type II) is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

The mode of preparation, Characters, Test for Identity, Tests for Purity, Assay, Storage, Labelling and Doses are the same as for Antipneumococcus Serum (Type I) with

the modification that suitable strains of *Diplococcus pneumoniæ* (*type II*) are used in the preparation and Assay of the serum.

SODII CITRAS

Sodium Citrate

Page 393,

delete the last two lines, and

Page 394,

delete lines 1–3;

insert "**Tests for Purity.** 2 grammes, boiled with 25 millilitres of *water* and cooled, requires for neutralisation not more than 0·5 millilitre of either *N/10 sulphuric acid*, or *N/10 sodium hydroxide, solution of thymol blue* being used as indicator (limit of alkalinity, or of acidity).".

SODII HYDROXIDUM

Sodium Hydroxide

Page 395,

after line 33,

insert "It contains not more than 2·5 per cent. of Na_2CO_3.".

line 38,

delete "Soluble in 1 part of *water*";

insert "Completely, or almost completely, soluble in 1 part of *water*".

Page 396, lines 1–7,

delete the test for "limit of carbonate".

after line 12,

insert "0·5 gramme, dissolved in *water* with the addition of 1·8 millilitres of *nitric acid*, complies with the *limit test for chlorides*. 1 gramme, dissolved in *water* with the addition of 3·5 millilitres of *hydrochloric acid*, complies with the *limit test for sulphates*.".

delete lines 15–19;

insert "**Assay.** Dissolve about 2 grammes, accurately weighed, in 25 millilitres of *water*, add 5 millilitres of *solution of barium chloride*, and titrate with *N/1 hydrochloric acid*, using *solution of phenolphthalein* as indicator.

To the solution in the flask add *solution of bromophenol blue*, and continue the titration with *N/1 hydrochloric acid*. Each millilitre of *N/1 hydrochloric acid* used in the second titration is equivalent to 0·0530 gramme of Na_2CO_3.

Each millilitre of *N/1 hydrochloric acid* used in the combined titrations is equivalent to 0·0400 gramme of total alkali, calculated as NaOH.".

SODII PHOSPHAS

Sodium Phosphate

Page 398,

after line 35,

insert "Dissolve 2 grammes in 20 millilitres of *water*, add 5 millilitres of *acetic acid* and 3 millilitres of *solution of calcium chloride*, and set aside for one hour; no turbidity is produced (absence of fluorides).".

SODII THIOSULPHAS

[Sod. Thiosulph.]

Sodium Thiosulphate

$Na_2S_2O_3,5H_2O$ . . . . Mol. Wt. 248·2

Sodium Thiosulphate may be prepared by the action of sulphur on sodium sulphite. It contains not less than 99 per cent., and not more than the equivalent of 101 per cent., of $Na_2S_2O_3,5H_2O$.

Characters. Colourless, transparent, monoclinic, prismatic crystals; odourless; taste, saline. Efflorescent in warm dry air; slightly deliquescent in moist air.

Soluble in 0·5 part of *water* at 25°; insoluble in *alcohol (95 per cent.)*.

Tests for Identity. Yields the *reactions* characteristic of sodium, and of thiosulphates.

Tests for Purity. A 10 per cent. w/v solution in *water* is neutral, or faintly alkaline, to *litmus*.

To 5 millilitres of a 5 per cent. w/v aqueous solution add 5 millilitres of *solution of ammonium oxalate*, and set aside for five minutes; no turbidity is produced (limit of calcium).

Arsenic limit, 2 parts per million. *Lead limit*, 5 parts per million.

Assay. Dissolve about 1 gramme, accurately weighed, in 20 millilitres of *water*, and titrate with *N/10 iodine*. Each millilitre of *N/10 iodine* is equivalent to 0·02482 gramme of $Na_2S_2O_3, 5H_2O$.

Storage. Sodium Thiosulphate should be kept in a well-closed container.

Sterilisation of a Solution. A solution of Sodium Thiosulphate for injection is sterilised by *heating in an autoclave*, or by *Tyndallisation*, or by *filtration*.

DOSES

Metric.	Imperial.
By subcutaneous, intramuscular or intravenous injection.	
0·3 to 1 gramme.	**5 to 15 grains.**

SULPHARSPHENAMINA

Sulpharsphenamine

Page 414, line 24,

delete "5";

insert "1·5".

Page 415,

after line 9,

insert "The solution is used immediately after preparation.".

THEOPHYLLINA

[Theophyll.]

Theophylline

$C_7H_8O_2N_4,H_2O$ . . . Mol. Wt. 198·1

Theophylline, 1 : 3 dimethylxanthine, is an alkaloid, obtained from the dried leaves of *Camellia sinensis* (Linn.) O. Kuntze; or it may be prepared synthetically.

Characters. A white, crystalline powder; odourless; taste, bitter.

Soluble in 120 parts of *water* at 25°, more soluble in hot *water*; soluble in 80 parts of *alcohol* (*95 per cent.*) at 25°; sparingly soluble in *ether*.

Tests for Identity. Dissolve 0·01 gramme in 1 millilitre of *hydrochloric acid*, add 0·1 gramme of *potassium chlorate*, and evaporate to dryness in a porcelain dish; a reddish residue remains, which becomes purple when exposed to the vapour of *dilute solution of ammonia*.

A cold saturated aqueous solution gives with *solution of tannic acid* a white precipitate, which is soluble in excess of the reagent.

Tests for Purity. *Melting-point*, 269° to 272°.

A saturated aqueous solution is neutral to *litmus*.

0·2 gramme, dissolved in 5 millilitres of *solution of potassium hydroxide*, or in 5 millilitres of *dilute solution of ammonia*, gives a clear solution (limit of caffeine, theobromine, and paraxanthine).

Dissolve 0·1 gramme in 2 millilitres of *sulphuric acid*; the solution is colourless; and dissolve 0·1 gramme in 2 millilitres of *nitric acid*; the solution is colourless (limit of readily carbonisable substances).

0·2 gramme loses, when dried at 100°, not more than 0·019 gramme; and leaves, on incineration, not more than 0·0002 gramme of residue.

Preparation. Injection of Mersalyl.

THYROIDEUM

Thyroid

Page 433, lines 26–28,

delete " and not more inorganic iodine than 10 per cent. of the content of total iodine.".

Page 434,

delete lines 8–42;

insert "**Assay.** Boil 1 gramme with 10 millilitres of *N/1 sodium hydroxide* under a reflux condenser for four hours; add 30 millilitres of *water* and, after cooling to about 40°, 11 millilitres, or a sufficient quantity, of *N/1 sulphuric acid* until the mixture is slightly acid to *Congo-red paper*. Set aside for eighteen to twenty-four hours, and filter through a filter paper, 45 millimetres in diameter, which has been accurately fitted to a funnel, the filter being finally drained by means of a suction pump. Transfer the filter paper with the contents to a nickel crucible, about 18 milli-

metres in diameter, sprinkle a little *anhydrous sodium carbonate* on the surface of the precipitate, and dry at 110°. Crumple up the filter paper, embed it completely in *anhydrous sodium carbonate* in the crucible, and complete the Assay as directed under 'Thyroxin-sodium', commencing with the words 'invert the crucible', and using for the final titration *N/200 sodium thiosulphate* in place of *N/20 sodium thiosulphate*. Each millilitre of *N/200 sodium thiosulphate* is equivalent to 0·1058 milligram of iodine in combination as thyroxine.".

THYROXINSODIUM

Thyroxine-sodium

Page 435,

delete lines 23–41, and

Page 436,

delete lines 1 and 2;

insert "**Assay.** Mix in a nickel crucible, approximately 18 millimetres in diameter, about 0·05 gramme, accurately weighed, with about 1 gramme of *anhydrous sodium carbonate*; fill the crucible completely with *anhydrous sodium carbonate*, well pressed down; invert the crucible and contents into a nickel crucible, 25 millimetres in diameter, and add sufficient *anhydrous sodium carbonate* to seal the junction of the two crucibles. Heat for fifteen minutes over a Bunsen flame in such a manner that the outer crucible is at a uniform dull red heat; allow to cool, break up the contents of the crucibles, place in a 250-millilitre beaker, add 100 millilitres of *water*, and boil gently for ten minutes. Filter, and wash the residue with a little *water*; boil the residue a second time with 100 millilitres of *water* for twenty minutes, again filter, and wash the residue with a little *water*. Transfer the mixed filtrates and washings to a 1 litre flask, cool, and add sufficient *water* to produce about 500 millilitres. Add 3 drops of *solution of methyl orange*, and sufficient *sulphuric acid* (*50 per cent. v/v*) to neutralise the solution. Then add 1 millilitre of *sulphuric acid* (*50 per cent. v/v*), 0·2 millilitre of *bromine* and a small piece of *marble* (about 0·05 gramme), and boil briskly for ten minutes. Cool to about 20°, add 0·2 millilitre of a 25 per cent. w/v solution of *phenol* in *glacial acetic acid*, and allow to stand for at least two minutes. Add 5 millilitres of *solution of potassium iodide*, and titrate with *N/20 sodium thiosulphate*, using at the end of the titration *mucilage of starch* as indicator. Each millilitre of *N/20 sodium thiosulphate* is equivalent to 1·058 milligrams of I.".

TINCTURA DIGITALIS
Tincture of Digitalis

Page 443, line 29,
delete "0·1";
insert "0·08".
Page 444, line 10,
delete "100";
insert "80".
after line 14,
insert "or alternatively:—

Powdered Digitalis—A quantity containing 1000 Units of activity, equivalent to 80 grammes of the *international standard digitalis powder.*

Alcohol (70 per cent.) . . 1000 millilitres

Macerate in a closed vessel for two days, shaking occasionally; strain; press the marc lightly; mix the liquids obtained. Clarify by subsidence, or by filtration.".

TINCTURA IPECACUANHÆ
Tincture of Ipecacuanha

Page 445,
after line 32,
insert "Dilute Acetic Acid . 16·5 millilitres".
line 37,
after "Alcohol (90 per cent.)",
insert "and the Dilute Acetic Acid".

TINCTURA STRAMONII
Tincture of Stramonium

Page 454,
delete lines 1–8;
insert

"Liquid Extract of Stramonium 100 millilitres
Alcohol (45 per cent.), sufficient
to produce . . . . 1000 millilitres

Mix; set aside for not less than twelve hours; filter.".

TOXINUM DIPHTHERICUM DETOXICATUM

Diphtheria Prophylactic

Page 461,

after line 15,

insert "(*f*) Alum Precipitated Toxoid, a suspension of white, slightly yellow or yellowish-brown particles in a colourless liquid, prepared by treating the filtrate with formaldehyde, adding Alum in the proportion necessary to produce a suitable precipitate, separating the precipitate, and washing and suspending it in Physiological Solution of Sodium Chloride.".

Page 461,

delete lines 34–44, and

Page 462,

delete lines 1–6;

insert "*Test II.* A quantity not exceeding five times the volume indicated as the adult dose injected under the skin on one occasion, or one-tenth of the volume indicated as the adult dose injected under the skin on two occasions, which are separated by an interval of not more than four weeks, into each of not less than ten normal guinea-pigs, gives them a degree of immunity indicated by the result of the following method of examination :—

One test dose of Schick Test Toxin is injected into the skin of each of the guinea-pigs; if ten guinea-pigs are used in the test, a "positive Schick reaction" must not occur in more than two of the animals; if more than ten guinea-pigs are used in the test a "positive Schick reaction" must not occur in more than one fourth of the animals tested.

For Diphtheria Toxin-Antitoxin Floccules and Diphtheria Toxoid-Antitoxin Floccules the test for potency as an immunising antigen may be carried out by the following alternative method :— A quantity not exceeding five times the volume indicated as the adult dose injected under the skin on one occasion, or one-tenth of the volume indicated as the adult dose injected under the skin on two occasions, which are separated by an interval of not more than four weeks, into each of not less than nine normal guinea-pigs gives them a degree of immunity indicated by the results of the following method of examination :—

One test dose of Schick Test Toxin and two test doses of Schick Test Toxin respectively are injected simultaneously at different places in the skin of each of the guinea-pigs; a positive reaction

to one Schick Test Dose must not occur in more than one-third of the animals tested or, alternatively, a positive reaction to two Schick Test Doses must not occur in more than two-thirds of the animals tested.

This examination is made not later than six weeks after the single injection and not later than three weeks after the second of the two injections.".

TRYPARSAMIDUM

[Tryparsamid.]

Tryparsamide

$NaO(OH)\cdot AsO\cdot C_6H_4\cdot NH\cdot CH_2\cdot CONH_2, \frac{1}{2}H_2O$

Mol. Wt. 305·0

Tryparsamide is sodium N-phenylglycineamide-*p*-arsonate, and may be prepared by boiling an aqueous solution of sodium-*p*-aminophenylarsonate with chloracetamide, converting the resulting N-phenylglycineamide-*p*-arsonic acid into its sodium salt, and crystallising from dilute alcohol. It contains not less than 25·1 per cent., and not more than 25·5 per cent., of As in organic combination, and not less than 9·25 per cent., and not more than 9·5 per cent., of N, both calculated with reference to the substance dried at 110°.

Characters. A colourless, crystalline powder; odourless.

Freely soluble in *water*; insoluble, or only slightly soluble, in *alcohol* (*95 per cent.*), in *ether*, in *chloroform*, and in *benzene*.

Tests for Identity. To the solution obtained in the Assay add *dilute sulphuric acid* and a slight excess of *sulphur dioxide*; boil until the odour of sulphur dioxide is removed, and pass in *hydrogen sulphide*; a yellow precipitate, which is soluble in *solution of ammonium carbonate*, is produced.

Dissolve 0·5 gramme in 5 millilitres of *water*, add 3 millilitres of *solution of sodium hydroxide*, and boil; ammonia is evolved.

To 1 millilitre of a 10 per cent. w/v aqueous solution add 1 millilitre of *solution of calcium chloride*; a precipitate of microscopic wedge-shaped prisms is gradually produced.

To 1 millilitre of a 10 per cent. w/v aqueous solution add 1 millilitre of *solution of silver nitrate*; a precipitate of thin microscopic needles is produced.

Tests for Purity. An aqueous solution is neutral to *litmus*.

To 1 millilitre of a 10 per cent. w/v aqueous solution add

1 millilitre of *solution of magnesium ammonio-sulphate*; no precipitate is produced in the cold (absence of arsenate, and of phosphate).

To 0·5 gramme in a test-tube (A), add 1 millilitre of *solution of arsanilic acid*. To 0·25 gramme in a test-tube (B), add 2 millilitres of *solution of arsanilic acid*. To each tube add 4 millilitres of *water* and 1·5 millilitres of a 1 per cent. w/v aqueous solution of *sodium nitrite*. Cool the tubes below 5°, and to each add 5 millilitres of *dilute hydrochloric acid* and 10 millilitres of *solution of β-naphthol*; the colour in tube A is not deeper than that in tube B (limit of arsanilic acid).

To 1 millilitre of a 10 per cent. w/v aqueous solution add 0·2 millilitre of *test-solution of ferric chloride*; a brown precipitate soluble in excess of *test-solution of ferric chloride* is formed, but no blue colouration is produced (absence of arsphenamine compounds).

Dissolve 3 grammes in 10 millilitres of *water*; the solution is free from suspended matter, and remains clear for six hours.

Loses, when dried at 110°, not less than 2·5 per cent., and not more than 3·5 per cent., of its weight.

Assay. *For arsenic.* Transfer about 0·2 gramme, accurately weighed, to a 600-millilitre conical flask, and moisten with 7·5 millilitres of *sulphuric acid*; add 1·5 millilitres of *fuming nitric acid*, and heat at about the boiling-point for forty-five minutes. Remove the flask from the source of heat, add 0·5 millilitre of *fuming nitric acid*, and heat until brown fumes cease to be evolved. Allow to cool slightly, and add in several portions 5 grammes of *ammonium sulphate*, and again heat gently, shaking occasionally until the evolution of gas has ceased. The resulting liquid should be colourless. Cool, and add sufficient *water* to produce 100 millilitres. Add 1 gramme of *potassium iodide*, boil gently until the volume is reduced to about 40 millilitres, cool, decolourise with *N/10 sodium thiosulphate*, and dilute with about 150 millilitres of *water*. Make the solution faintly alkaline to *litmus* with *solution of sodium hydroxide*, and then faintly acid with *dilute sulphuric acid*, add 20 millilitres of a cold saturated solution of *sodium bicarbonate*, and titrate with *N/10 iodine*, using *mucilage of starch* as indicator. Each millilitre of *N/10 iodine* is equivalent to 0·003747 gramme of As.

For nitrogen. Dissolve about 0·3 gramme, accurately weighed, in 30 millilitres of *nitrogen-free sulphuric acid*, add 10 grammes of *potassium sulphate* and a small globule of *mercury*, and heat until a clear colourless liquid is obtained; cool, dilute with *water*, transfer to an ammonia distillation apparatus, add an excess of a 40 per cent. w/v solution of *sodium hydroxide* in *water* and 1 millilitre of *solution of sodium sulphide*, and

distil the liberated ammonia into 25 millilitres of *N/10 sulphuric acid*; titrate the excess of acid with *N/10 sodium hydroxide*, using *solution of methyl red* as indicator. Each millilitre of *N/10 sulphuric acid* is equivalent to 0·0014 gramme of N.

Storage. Tryparsamide should be kept in a small well-closed container, protected from light, and stored in a cool place.

Sterilisation of a Solution. Tryparsamide is prepared in sterile solution for injection by dissolving it in the requisite amount of Sterilised Water.

DOSES

Metric.	Imperial.
By subcutaneous, intramuscular or intravenous injection.	
1 to 2 grammes.	**15 to 30 grains.**

NOTE.—In Canada Tryparsamide will be controlled by patents until the 2nd November, 1938.

UNGUENTUM SIMPLEX

Simple Ointment

Page 476, line 12,

before " When Simple Ointment ",

insert " Unless otherwise directed in the text,".

UNGUENTUM SULPHURIS

Ointment of Sulphur

Page 476, line 20,

after " Simple Ointment ",

insert ", prepared with White Soft Paraffin ".

VALERIANA

Valerian

Page 481, line 9,

delete " 10 ";

insert " 12 ".

ZINCI SULPHAS

Zinc Sulphate

Page 484, line 36,

after "bottle",

insert ", add 5 millilitres of *water*, and shake well".

line 37,

after "titrate",

insert "immediately".

APPENDICES

APPENDIX		PAGE
I	MATERIALS AND SOLUTIONS EMPLOYED IN TESTS	75
II	VOLUMETRIC DETERMINATIONS :—	
	A. SOLUTIONS EMPLOYED IN VOLUMETRIC DETERMINATIONS	78
	B. INDICATORS EMPLOYED IN VOLUMETRIC DETERMINATIONS AND IN *p*H DETERMINATIONS	79
IV	DETERMINATION OF—	
	A. FREEZING-POINT, MELTING-POINT, AND SOLIDIFYING-POINT	79
	D. OPTICAL ROTATION	79
	F. VISCOSITY	79
	G. ULTRA-VIOLET ABSORPTION	81
V	QUALITATIVE REACTIONS AND TESTS FOR SUBSTANCES MENTIONED IN THE PHARMACOPŒIA	82
VI	QUANTITATIVE TEST FOR LEAD	82
VII	QUANTITATIVE TEST FOR ARSENIC	82
XI	DETERMINATION OF—	
	A. ESTERS IN VOLATILE OILS	83
	D. CARVONE IN OIL OF CARAWAY, AND IN OIL OF DILL	83
XIV	COLOUR GLASSES FOR THE SULPHURIC ACID TEST ON LIQUID PARAFFIN	84
XV	BIOLOGICAL ASSAYS :—	
	A. ANTIRACHITIC VITAMIN (VITAMIN D)	84
	D. GAS-GANGRENE ANTITOXIN (PERFRINGENS)	86
	I. POWDERED DIGITALIS	86
	O. VITAMIN A (INCLUDING THE SPECTROPHOTOMETRIC METHOD)	86
	P. ANTINEURITIC VITAMIN (VITAMIN B_1)	91
	Q. ANTISCORBUTIC VITAMIN (VITAMIN C)	93
	R. ANTIPNEUMOCOCCUS SERUM (TYPE I)	97
	S. ANTIPNEUMOCOCCUS SERUM (TYPE II)	102
	T. GAS-GANGRENE ANTITOXIN (ŒDEMATIENS)	102
	U. GAS-GANGRENE ANTITOXIN (VIBRION SEPTIQUE)	106
	V. STAPHYLOCOCCUS ANTITOXIN	111

XVI SPECIAL PROCESSES USED IN PREPARING SOLUTIONS FOR INJECTION :—
A. METHODS OF STERILISING 117
C. TESTS FOR LIMIT OF ALKALINITY OF GLASS . 118

XXI WEIGHTS AND MEASURES OF THE BRITISH PHARMACOPŒIA 118

APPENDICES

APPENDIX I

MATERIALS AND SOLUTIONS EMPLOYED IN TESTS

Page 494,

delete line 15;

insert "**Arachis Oil**: of the British Pharmacopœia.

Arsanilic Acid: para-arsanilic acid, $NH_2 \cdot C_6H_4 \cdot AsO(OH)_2$, of Reagent purity.

Arsanilic Acid, Solution of: dissolve 0·005 gramme of *arsanilic acid* in 20 millilitres of *water* by the addition of a few drops of *solution of sodium hydroxide*, and add a sufficient quantity of *water* to produce 100 millilitres.".

Page 495, after line 9,

insert "**Calcium Acid Phosphate**: $CaHPO_4,2H_2O$, of Reagent purity.".

after line 18,

insert "**Calcium Lactate**: of the British Pharmacopœia.".

Page 498, after line 4,

insert "**Cottonseed Oil**: of the British Pharmacopœia.".

after line 10,

insert "**Cyclohexane**: C_6H_{12}, a clear colourless liquid, *specific gravity* (15·5°/15·5°), about 0·78; *boiling-point*, 81° to 82°; *freezing-point*, 4·5° to 6·5°; almost completely transparent to radiation of greater wave-length than 250mμ, and exhibits no trace of discontinuous absorption.".

after line 11,

insert "**2 : 6-Dichlorophenolindophenol**: $HO \cdot C_6H_4 \cdot N : C_6H_2Cl_2 : O$, of Reagent purity.

2 : 6-Dichlorophenolindophenol, Solution of: warm

0·1 gramme of *2 : 6-dichlorophenolindophenol* with 100 millilitres of *water*, and filter.

Solution of 2 : 6-Dichlorophenolindophenol must not be used later than three days after preparation.

Digitonin : of Reagent purity.".

delete lines 14–19 ;

insert " **Dimethylaminobenzaldehyde, Solution of :** dissolve 0·125 gramme of *dimethylaminobenzaldehyde* in a cooled mixture of 65 millilitres of *sulphuric acid* and 35 millilitres of *water*, and add 0·1 millilitre of *test-solution of ferric chloride*.

Solution of Dimethylaminobenzaldehyde must not be used later than seven days after preparation.".

after line 20,

insert " **3 : 5-Dinitrobenzoyl chloride :** $C_6H_3(NO_2)_2 \cdot COCl$, of Reagent purity.

Diphenylbenzidine : $C_6H_5 \cdot NH \cdot C_6H_4 \cdot C_6H_4 \cdot NH \cdot C_6H_5$, of Reagent purity.".

after line 22,

insert " **Eosin :** the di-sodium salt of tetrabromofluorescein, $C_{20}H_6Br_4O_5Na_2$, of Reagent purity.

Eosin, Solution of : a 0·5 per cent. w/v solution of *eosin* in *water*.".

Page 499, after line 21,

insert " **Formic Acid :** of Reagent purity, containing about 90 per cent. w/w of HCOOH.

Fuller's Earth : of commerce, complying with the following test :—Suspend 1 gramme in 80 millilitres of *water* and add 15 millilitres of a 1 per cent. w/v solution of *quinine bisulphate*. Set aside for half an hour, shaking occasionally, and filter. To 50 millilitres of the filtrate add 0·5 millilitre of *solution of potassio-mercuric iodide* ; any turbidity produced is not greater than the turbidity produced by diluting 0·5 millilitre of a 0·1 per cent. w/v solution of *quinine bisulphate* with *water* to 50 millilitres and adding 0·5 millilitre of *solution of potassio-mercuric iodide*.

after line 23,

insert " **Haematoxylin :** of Reagent purity.

Haematoxylin and Alum, Solution of : mix 10 millilitres of a 10 per cent. w/v solution of *haematoxylin* in *dehydrated alcohol* with 200 millilitres of a 10 per cent. w/v solution

of *alum* in *water*, and add 3 millilitres of a 6·25 per cent. w/v solution of *potassium permanganate* in *water*; boil for one minute, stirring constantly, and cool quickly.

Haematoxylin and Ferric Ammonium Sulphate, Solution of: pour, slowly and with stirring, 150 millilitres of a 6·6 per cent. w/v solution of *ferric ammonium sulphate* in *water* into 75 millilitres of a 2 per cent. w/v solution of *haematoxylin* in warm *water*, boil for half a minute, and allow to cool; filter before use.".

Page 501, after line 2,

insert "**Iron Citrate:** of commerce, scales.".

after line 18,

insert "**Magenta, Acid:** of Reagent purity.".

Page 502, after line 6,

insert "**Marble:** of Reagent purity.".

Page 503, after line 6,

insert "**β-Naphthol, Solution of:** dissolve 5 grammes of *β-naphthol*, freshly recrystallised, in 40 millilitres of *solution of sodium hydroxide*, and add sufficient *water* to produce 100 millilitres.

Solution of β-Naphthol must be freshly prepared.".

Page 504, after line 10,

insert "**Phenylhydrazine:** $C_6H_5{\cdot}NH{\cdot}NH_2$, of Reagent purity.".

after line 19,

insert "**Picrolonic Acid:** 1-(4-nitrophenyl)-3-methyl-4-nitropyrazolone(5), $C_{10}H_8O_5N_4$, of Reagent purity.".

Page 507, after line 9,

insert "**Potassium Phosphate:** Dipotassium hydrogen phosphate, K_2HPO_4, of Reagent purity.".

after line 17,

insert "**Pyridine:** C_5H_5N, of Reagent purity.".

after line 22,

insert "**Quinine Bisulphate:** of the British Pharmacopœia.".

after line 25,

insert "**Rice Starch:** of the British Pharmacopœia.".

Page 508, after line 23,

insert "**Sodium Caseinate**: Soluble casein of commerce, extracted with *alcohol* (*95 per cent.*) and *ether*.".

Page 509, after line 4,

insert "**Sodium Iodide**: of the British Pharmacopœia.".

Page 510, after line 33,

insert "**Sulphanilic Acid**: $C_6H_4NH_2SO_3H$, of Reagent purity.

Sulphur Dioxide: SO_2, of commerce.".

after last line,

insert "**Sulphuric Acid (50 per cent. v/v)**: Mix equal volumes of *sulphuric acid* and *water*, and cool.".

Page 511, line 6,

after "96 per cent. w/w of H_2SO_4",

insert ", and complying with the following test:—Mix 45 millilitres with 5 millilitres of *water*, cool, and add 8 milligrams of *diphenylbenzidine*; the solution is colourless, or not more than very pale blue.

Nitrogen-free Sulphuric Acid should be stored in small containers. Supplies which may have absorbed water or nitric acid from the air should be rejected.".

Page 512, before line 1,

insert "**Trinitrophenol and Acid Magenta, Solution of**: mix 5 millilitres of a 2 per cent. w/v solution of *acid magenta* in *water* with 100 millilitres of a saturated solution of *trinitrophenol* in *water*, and add immediately before use 0·5 millilitre of a 1 per cent. solution of *glacial acetic acid* in *water*.".

APPENDIX II

A. *SOLUTIONS EMPLOYED IN VOLUMETRIC DETERMINATIONS*

Page 513, before line 1,

insert "**Solution of Barium Hydroxide, N/10.**

Barium hydroxide, dissolved in freshly boiled and cooled *water* to contain in 1000 millilitres 15·775 grammes of $Ba(OH)_2,8H_2O$.",

B. *INDICATORS EMPLOYED IN VOLUMETRIC DETERMINATIONS AND IN pH DETERMINATIONS*

Page 519, line 4,

delete "*alcohol* (*20 per cent.*)";
insert "*alcohol* (*50 per cent.*)".

APPENDIX IV

A. *DETERMINATION OF FREEZING-POINT, OF MELTING-POINT, AND OF SOLIDIFYING-POINT*

VI. *Solidifying-point of the Fatty Acids in Soaps.*

Page 530, line 35,

delete "30";
insert "15".

D. *DETERMINATION OF OPTICAL ROTATION*

Page 538, last line,

after "solution",
insert "at 20°. The specific rotation, unless otherwise stated, is calculated from observations made with sodium light. For certain substances the observations are made with the light from a mercury vapour lamp, using the green line of wave-length 546·1 millimicron (mμ).".

F. *DETERMINATION OF VISCOSITY*

Page 539,

delete lines 11–39;
insert "The dynamic viscosity (η) of a liquid in units of the centimetre-gramme-second system is the tangential force in dynes per square centimetre exerted on each of two parallel planes, placed 1 centimetre apart in the liquid, when one of the planes is moving in its own plane with a velocity of 1 centimetre per second relatively to the other. The unit of dynamic viscosity on the centimetre-gramme-second system, the poise, is the dynamic viscosity of a liquid in which the force between the two planes is 1 dyne per square centimetre. The centipoise is one-hundredth of a poise.

The kinematic viscosity (ν) of a liquid is the quotient obtained by dividing the dynamic viscosity by the density of the liquid. The unit of kinematic viscosity on the centimetre-gramme-second system, the stokes, is the kinematic viscosity of a liquid which has a dynamic viscosity of 1 poise

and a density of 1 gramme per cubic centimetre.[1] The centistokes is one-hundredth of a stokes.

Viscosity is determined by means of a glass viscometer of the type, shown in the figure, and constructed in accordance with the dimensions shown in the tables. The specification of the apparatus and method of procedure is in agreement with the British Standard Specification No. 188, 1929.".

Page 540,

before line 1,

insert "TABLE I

DIMENSIONS OF VISCOMETERS SUITABLE FOR LIQUID PARAFFIN

Range = 30 to 250 centistokes.
Length of Tube (aB) = 7 cm.
Length of Capillary (de) = 10 cm.

All linear dimensions are given in centimetres.
All volumes are given in millilitres.

Capillary (de): internal diameter	0·24	0·25	0·22	0·20	0·19	0·18
Tube (aB): internal diameter	0·7	0·7	0·7	0·7	0·7	0·7
Bulb (BC) { internal diameter	2·8	2·6	2·4	2·2	2·1	1·9
Bulb (BC) { capacity	20·0	16·2	13·2	10·4	8·2	6·4
Bulb (Cd): capacity	1·2	1·2	1·2	0·6	0·6	0·6
Bent tube (ef): minimum internal diameter	0·7	0·7	0·7	0·7	0·7	0·7
Tube (Gh): internal diameter	0·7	0·7	0·7	0·7	0·7	0·7
Bulb (fG) { minimum internal diameter	2·8	2·6	2·4	2·2	2·1	2·0
Bulb (fG) { minimum capacity	21·5	18·0	15·0	11·5	9·0	7·5
Dimension *x*	5·7	5·5	5·3	5·1	5·0	4·9
Distance between vertical axes	2·1	2·0	1·8	1·6	1·5	1·4
Vertical distance of M above G	0·12	0·12	0·12	0·15	0·15	0·15

[1] In actual determinations densities expressed in grammes per millilitre may be employed, since the difference between the cubic centimetre and the millilitre is too small to affect the results significantly.

TABLE II

DIMENSIONS OF VISCOMETERS SUITABLE FOR A 3 PER CENT. SOLUTION OF PYROXYLIN IN ACETONE".

Page 540, line 1,

delete "1·9 to 15 poises";

insert "200 to 1500 centistokes".

delete lines 29–42;

insert "METHOD OF PROCEDURE.—The viscometer is filled to the marks M and G with the liquid to be tested and is placed vertically in a bath maintained at the specified temperature. The liquid is sucked, or blown, up to a point 1 centimetre above B, and the time taken for the meniscus to fall from mark B to mark C is measured.

The constant (K) of the instrument is determined in centistokes per second by observations on a liquid of known kinematic viscosity.

The kinematic viscosity is calculated from the equation

$$\nu = Kt$$

where ν = kinematic viscosity in centistokes

t = time in seconds for the meniscus to fall from B to C.

The dynamic viscosity is calculated from the equation

$$\eta = \nu\rho$$

where η = dynamic viscosity in poises

ρ = weight in grammes of 1 millilitre of the liquid at the temperature of the test.".

Page 540, after last line,

insert

"G. *DETERMINATION OF ULTRA-VIOLET ABSORPTION*

The ultra-violet absorption is the logarithm of the ratio of the intensities of the incident and emergent beams of ultra-violet radiation of a specified wave-length, when allowed to pass through a layer, 1 centimetre in thickness, of a 1 per cent. w/v solution of the substance in a specified solvent. The ratio of the intensities is measured in a spectrophotometer by a photographic, or other suitable, method.".

APPENDIX V

QUALITATIVE REACTIONS AND TESTS FOR SUBSTANCES MENTIONED IN THE PHARMACOPŒIA

Page 549, after line 12,

insert "Thiosulphates

Solutions of thiosulphates give with *hydrochloric acid* a white precipitate of sulphur, which soon turns yellow, and evolve sulphur dioxide, a colourless gas with a pungent smell of burning sulphur.

Strong solutions of thiosulphates give with *solution of barium chloride* a white precipitate, which is soluble in *hydrochloric acid* with separation of sulphur.

Solutions of thiosulphates decolourise *solution of iodine*; the decolourised solution does not give the *reaction* for sulphates.

Solutions of thiosulphates decolourise *solution of bromine*; the decolourised solution gives the *reaction* for sulphates.".

APPENDIX VI

QUANTITATIVE TEST FOR LEAD

Table, page 554,

insert "Calcii Gluconas . | 7 | 5 | 2 | 5 | 5 | **10** ".

Page 558,

insert "Sodii Thiosulphas . | 12 | — | 2 | — | 5 | **5** ".

APPENDIX VII

QUANTITATIVE TEST FOR ARSENIC

Page 566, after last line,

insert "Bismuthi et Sodii Tartras.

Limit **2** parts per million.

Treat **5** grammes as described under 'Bismuthi Salicylas'.

Bismuthi Oxychloridum.

Limit **2** parts per million.

Treat **5** grammes as described under '**Bismuthi Carbonas**'.".

Page 567, after line 26,

insert "**Calcii Gluconas.** Limit **5** parts per million.

Treat **2** grammes as described under '**Calcii Lactas**'.".

Page 568, after line 23,

insert "**Ferri Subchloridum Citratum.**

Limit **10** parts per million.

Treat **1** gramme as described under '**Ferri Carbonas Saccharatus**'.".

Page 570, after line 32,

insert "**Mersalylum.** Limit **10** parts per million.

Mix **1** gramme with 1 gramme of *calcium hydroxide As T.* and 1 millilitre of *water*, dry and ignite gently; dissolve the residue in 14 millilitres of *brominated hydrochloric acid As T.* and 45 millilitres of *water*, and remove the excess of bromine by a few drops of *solution of stannous chloride As T.*".

Page 573, after line 11,

insert "**Sodii Thiosulphas.** Limits **2** parts per million.

Boil **5** grammes with 5 grammes of *potassium chlorate As T.* and 35 millilitres of *water*, until dissolved; add 18 millilitres of *hydrochloric acid As T.*, and continue boiling gently, until the reaction is complete and most of the chlorine is evolved; cool, add 15 millilitres of *water* and a few drops of *stannous chloride solution As T.*".

APPENDIX XI

A. *DETERMINATION OF ESTERS IN VOLATILE OILS*

Page 580, after line 20,

insert "0·1311 gramme of Santalyl Acetate".

D. *DETERMINATION OF CARVONE IN OIL OF CARAWAY, AND IN OIL OF DILL*

Page 583, line 17,

delete "**about thirty-five**";
insert "**forty**".

APPENDIX XIV

Pages 596 and 597,

delete this appendix;
insert

APPENDIX XIV

COLOUR GLASSES FOR THE SULPHURIC ACID TEST ON LIQUID PARAFFIN

The colour glasses are standardised to have the following properties on the system of colour measurement adopted at the National Physical Laboratory, Teddington.

Red glass :
Colour Quality : 0·377 X + 0·33 Y + 0·292 Z
Photometric Transmission : 66·6 per cent.

Yellow glass :
Colour Quality : 0·412 X + 0·451 Y + 0·137 Z
Photometric Transmission : 84·3 per cent.

Combination of the Red glass and the Yellow glass :
Colour Quality : 0·447 X + 0·423 Y + 0·130 Z
Photometric Transmission : 56·2 per cent.

In the foregoing specifications, X, Y and Z denote the reference stimuli of the system of colour specification adopted by the International Commission on Illumination, in 1931, and the measurements, both of colour quality and photometric transmission, are presumed to be made with source B, adopted by that Commission for colorimetric measurements.

APPENDIX XV

A. *BIOLOGICAL ASSAY OF ANTIRACHITIC VITAMIN (VITAMIN D)*

Page 599, lines 4 and 5,

delete "A suitable dose of the Standard Preparation is about 0·25 Unit.";
insert "Suitable doses of the Standard Preparation may vary from 0·25 to 1 Unit.".

Page 599, line 6,
delete " receives " ;
insert " may receive ".

after line 8,
insert " Alternatively, the whole of the ten days' dose may be given as one dose at the beginning of the test period.".

line 34,
delete " difference " ;
insert " ratio ".

line 36,
delete " difference " ;
insert " relation ".

lines 38 and 39,
delete " A difference of 50 per cent., or more, in potency can be detected by this test.".
insert " Limits of Error :—When the method of X-ray examination is used, in an experiment in which 10 rats are used in each group and the litters are evenly divided between the groups, the limits of error (P = 0·99) are 63 and 159 per cent.
When the method of examination of the bones after staining is used, and there is a severe initial degree of rickets, the limits of error (P = 0·99) are 49 and 215 per cent.".

Page 600, lines 4 and 5,
delete " A suitable dose of the Standard Preparation is about 0·1 Unit." ;
insert " Suitable doses of the Standard Preparation may vary from 0·025 to 0·1 Unit.".

line 9,
after " bones ",
insert " , e.g. femora or humeri,".

line 14,
after " are ",
insert " dried,".

line 16,
before " bone ",
insert " dry extracted ".

after line 31,
insert " Limits of Error :—In an experiment in which

10 rats receive the Standard Preparation and 10 rats receive the preparation being tested, and the litters are evenly divided between the two groups, the limits of error (P = 0·99) are 59 and 170 per cent.".

D. *BIOLOGICAL ASSAY OF GAS-GANGRENE ANTITOXIN (PERFRINGENS)*

Page 607, line 25,
after " Gas-gangrene Antitoxin ",
insert " (perfringens) ".

I. *BIOLOGICAL ASSAY OF POWDERED DIGITALIS*

Page 620, line 28,
delete " 0·1 " ;
insert " 0·08 ".

Page 623, line 14,
delete " 10 " ;
insert " 8 ".

Page 624, line 17,
delete " 10 " ;
insert " 8 ".

O. *ASSAY OF VITAMIN A*

The activity of a preparation of vitamin A is determined by comparing its activity by a suitable biological method with that of the Standard Preparation of Vitamin A, or with that of a subsidiary laboratory standard, the activity of which is known in terms of the Standard Preparation.

An expression of the content of vitamin A in a preparation may be obtained by multiplying the *ultra-violet absorption* by a factor.

1. Standard Preparation of Vitamin A.

The Standard Preparation for Great Britain and Northern Ireland is a quantity of pure β-carotene kept in the National Institute for Medical Research, Hampstead, London. The Standard Preparation for other parts of the British Empire is the same, except for those countries in which a similar standard preparation, kept in a different institute, has been defined by law ; in these countries the standard preparation, so defined, is used.

2. The Unit of Vitamin A.

The Unit of Vitamin A activity for Great Britain and Northern Ireland is the same as the international unit. It is defined as the specific activity contained in 0·6 microgram (0·6γ) of the Standard Preparation of pure β-carotene. The Unit for other parts of the British Empire is the same, except for those countries in which a similar unit has been defined by law; in these countries the unit, so defined, is used.

3. Suggested Details of Biological Method.

(*a*) *Increase in weight in rats which have ceased to grow on a diet deficient in vitamin A.* Four or five litters, containing in all about 30 newly-weaned rats, each weighing from 30 to 40 grammes, are used for the test. They are given a diet containing all essentials for growth except vitamin A, until their reserves of that factor are exhausted and they cease to grow. This takes place in four to five weeks, if the stock from which the rats are drawn has been fed on a diet containing only a moderate amount of vitamin A. The diet used for this test may consist of:—

Sodium caseinate	15 per cent.
Rice starch (preferably partially dextrinised)	73 per cent.
Dried brewer's yeast . . .	8 per cent.
Salt mixture	4 per cent.

The following is a suitable salt mixture for use in preparing this diet:—

Sodium chloride	23·4 parts
Magnesium sulphate	24·6 „
Sodium phosphate	35·8 „
Potassium phosphate	69·6 „
Calcium acid phosphate . . .	68·8 „
Calcium lactate	15·4 „
Iron citrate	6·0 „
Potassium iodide	0·2 „

In addition each rat receives about 10 Units of Vitamin D per week, given in one dose as one or more drops of a suitable

solution directly into the mouth. The diet may include also 15 per cent. of a vitamin A-free fat in place of 15 per cent. of starch; if this addition is made the vitamin D may be added to the fat. Fresh tap-water is supplied daily.

Each rat is weighed twice weekly. When three successive half-weekly weighings have shown that its weight has not increased by more than 2 grammes, it is allocated to one of four or five groups. The groups are arranged so as to include equal numbers from each litter and equal numbers of males and females. Two of the groups are used for testing two doses of the Standard Preparation (1 Unit and 3 Units are suitable doses), and the other two or three groups for testing two or three doses of the cod-liver oil being tested (0·5, 1·0 and 2·0 milligrams are suitable doses). Thus the rats of different groups receive different doses, but all the rats of any one group receive equal doses. The doses may be given daily, or only twice a week in equivalent amount, suitable solutions being made so that the required dose can be administered as one or more drops, directly into the mouth of the rat, which is held firmly in the palm of the operator's hand with its mouth open to receive the drop. The rats are weighed once a week for three weeks, or for longer if desired, but the degree of accuracy obtainable in a test lasting for four weeks is only slightly greater than that obtained in a test lasting for three weeks. At the end of this time, the average increases in weight of the rats in the different groups are determined. Comparisons are drawn between the groups receiving doses of the cod-liver oil being tested and those receiving doses of the Standard Preparation, and the activity of the cod-liver oil being tested is calculated in terms of the Standard Preparation. The range of doses, proposed for the Standard Preparation and for the cod-liver oil being tested, will be suitable for samples of cod-liver oil, whose potencies range from about 500 Units per gramme (when the doses 2·0 milligrams of cod-liver oil and 1 Unit of the Standard Preparation give equal results) to about 6000 Units per gramme (when the doses 0·5 milligram of cod-liver oil and 3 Units of the Standard Preparation give equal results).

Only two groups of 10 rats each need be used, if the relation between average increase in weight and dose of vitamin A given has been previously determined. Every rat in one group may then receive 2 milligrams of the cod-liver oil being

tested, and every rat in the other group may receive 2 Units of the Standard Preparation. If these groups give equal average increases in weight, the potency of the oil is 1000 Units per gramme. If the two groups do not give equal increases in weight, the potencies of the doses are not directly proportional to the mean increases in weight, but to the amounts of vitamin A, which have been determined previously by the special experiment as corresponding to the two mean increases in weight.

Limits of Error:—In an experiment in which 10 rats (5 males and 5 females) receive the Standard Preparation and 10 rats (5 males and 5 females) receive the preparation being tested, and in which the mean responses are equal, the limits of error (P = 0·99) are 30 and 339 per cent. for a three weeks' test, and 37 and 272 per cent. for a five weeks' test.

(*b*) *Prophylactic.* The method described above can be carried out as a prophylactic test by giving doses of the preparation being tested and of the Standard Preparation to groups of rats, suitably arranged, from the beginning of the experiment instead of giving them only after the animals have become steady in weight. Certain modifications of the test are necessary:—(1) in every test observations must be made on a control group of rats which receive neither the cod-liver oil being tested nor the Standard Preparation; (2) the test must be carried on until this control group has died, and the other groups of rats, receiving different doses of the cod-liver oil being tested or of the Standard Preparation, show differences in average increases in weight; comparisons can then be drawn between these different groups; (3) a previous determination of the relation between increases in weight and doses of vitamin A cannot be used in order to reduce the number of groups of rats used. Doses suitable for a prophylactic test are about one-tenth of the doses suitable for a curative test.

Limits of Error:—The data at present available do not permit of the calculation of the error of this test. Individual workers should estimate the error from their own data.

4. Suggested Details of Spectrophotometric Method.

A solution of the unsaponifiable matter of the cod-liver oil in *dehydrated alcohol* or *cyclohexane* is prepared by the method described below, and the *ultra-violet absorption* at 328mμ is determined by means of a suitable spectrophotometer, the

result being calculated with reference to the original oil. An expression of the content of vitamin A in the cod-liver oil in Units per gramme is obtained by multiplying the *ultra-violet absorption* by the factor declared by the Permanent Commission on Biological Standardisation of the Health Organisation of the League of Nations as the factor to be used for this purpose.[1]

Preparation of the solution of the unsaponifiable matter.

Boil 1 gramme of the cod-liver oil with 10 millilitres of freshly prepared *N/2 alcoholic solution of potassium hydroxide* for five minutes, or until the solution is clear. Add 20 millilitres of *water*, transfer to a small separator, and extract with two successive quantities of 25 millilitres of *anæsthetic ether*. Wash the mixed ethereal solutions by gentle rotation, without violent shaking, successively with 10 to 20 millilitres of *water*, with 10 to 20 millilitres of *N/2 potassium hydroxide*, and with *water*. Again wash the ethereal solution by shaking thoroughly with two successive quantities of 10 millilitres of *water*, filter into a flask, remove the ether, and dissolve the residue in a sufficient quantity of *dehydrated alcohol* or *cyclohexane* to produce a solution of the concentration required for the instrument to be used. A preliminary test on the untreated oil will indicate the quantities of oil and of solvent, which will be necessary.

A statement of the vitamin A content which has been derived in this way should be accompanied by a statement indicating the method of assay employed.

The spectrophotometric method, as described, measures the amount of a substance having a certain physical property characteristic of vitamin A. When applied to the determination of vitamin A in a specimen of cod-liver oil, which conforms in all other respects to the Pharmacopœial requirements, it gives a trustworthy measurement, but it may be inapplicable in the presence of other substances showing absorption in the region of 328mμ. In the event of a discrepancy, due to this or any other cause, between the Units of vitamin A in a preparation of vitamin A, as determined by the biological method and by the spectrophotometric method, the value as determined by the biological method shall be accepted.

Limits of Error:—The limits of error (P = 0·99) for the actual physical measurement of the intensity of absorption

[1] The factor accepted at present (December, 1936) is 1600.

at 328mμ depend on the level of absorption and the number of replicate tests made.

The following table gives the values obtained under different conditions :—

Intensity of absorption $E^{1\ per\ cent.}_{1\ cm.}$	Single tests per cent.	Tests in duplicate per cent.	Tests in quadruplicate per cent.
0·33	80 and 120	86 and 114	90 and 110
0·67	90 and 110	93 and 107	95 and 105
1·33	95 and 105	96·5 and 103·5	97·5 and 102·5

No information is available for the calculation of the error of the factor.

P. *BIOLOGICAL ASSAY OF ANTINEURITIC VITAMIN (VITAMIN B_1)*

The activity of a preparation of antineuritic vitamin (vitamin B_1) is determined by comparing its antineuritic activity with that of the Standard Preparation of Antineuritic Vitamin (Vitamin B_1) by a suitable method.

1. Standard Preparation of Antineuritic Vitamin (Vitamin B_1).

The Standard Preparation for Great Britain and Northern Ireland is kept in the National Institute for Medical Research, Hampstead, London. The Standard Preparation for other parts of the British Empire is the same, except for those countries in which a similar standard preparation, kept in a different institute, has been defined by law ; in these countries the standard preparation, so defined, is used.

2. The Unit of Antineuritic Activity (Vitamin B_1).

The Unit of Antineuritic Activity (Vitamin B_1) for Great Britain and Northern Ireland is the same as the international unit and is defined as the specific antineuritic activity contained in 10 milligrams of the Standard Preparation. The Unit for other parts of the British Empire is the same, except for those countries in which a similar unit has been defined by law ; in these countries the unit, so defined, is used.

3. Suggested Details of Method.

Increase in weight of rats which have ceased to grow while receiving a diet deficient in vitamin B_1.

About 10 young rats, each weighing from 40 to 50 grammes, immediately after weaning, are fed upon a diet, which contains

all essentials for growth except vitamin B_1. A basal diet suitable for this test may consist of:—

Sodium caseinate	100 grammes
Rice starch	300 grammes
Arachis oil or *cottonseed oil*	75 grammes
Salt mixture (see Assay of Vitamin A, page 87)	25 grammes
Water	500 grammes

The well mixed diet should be thoroughly cooked by steaming for about three hours. Each rat receives daily 3 to 5 drops (0·06 to 0·1 gramme) of cod-liver oil from a dropping pipette to provide vitamins A and D. Vitamin B_2 may be provided by administration of 1 millilitre of an autoclaved extract of yeast, made as follows:—

Mix fresh pressed brewer's yeast with sufficient *water* to produce the consistency of cream, transfer to a filter, remove the liquid as completely as possible by suction, and complete the removal of liquid by means of a hand-press. Repeat this process with several successive quantities of *water* until the expressed liquid is of a pale straw colour. Determine the proportion of dry solids in the residue by drying a small quantity at 100°. Mix the quantity of residue, which corresponds to 100 grammes of dry solids, with from 1000 to 1500 millilitres of a boiling 0·02 per cent. w/v solution of *glacial acetic acid* in *water*, boil for five minutes, stirring constantly, and filter while hot. Evaporate the filtrate on a water-bath to 200 millilitres, and heat in an autoclave at 120° for five hours in order to destroy vitamin B_1.

The rats are placed in separate cages with wire grids of mesh not smaller than $^1/_3$ inch, in order to hinder access to fæces. The young rats thus fed show an increase in weight for two or three weeks, which then ceases. When the weight has been stationary for not less than five days or has begun to decline, the rats are divided into two groups. Each rat of one group receives daily for four weeks 10 milligrams of the substance being tested, and each rat of the other group receives daily for the same period 10 milligrams (1 Unit) of the Standard Preparation. The doses are readily taken, if moistened with water and given on a small dish. The average increase in weight of the rats is determined for each group.

If the average increase in weight is approximately the same for both groups, the vitamin B_1 activity of the substance being tested is equal to that of the Standard Preparation. If the increase in weight in the group receiving the substance being tested is less or greater than that in the group receiving the Standard Preparation, the test is repeated using a larger or smaller dose of the substance being tested, a simultaneous experiment being made with the Standard Preparation. Alternatively, for the first trial two doses of the substance being tested may be given, and fourteen rats may be used. In each trial there should be at least 2 rats receiving no dose; these should show a gradual decline in weight ending usually in convulsions, caused by vitamin B_1 deficiency.

The rats used in any one trial should be drawn from two or three litters, those receiving the different doses being evenly distributed over these litters.

The activity of the preparation being tested is calculated from the dose, which gives a result equal to that given by 1 Unit of the Standard Preparation.

Limits of Error:—In an experiment in which 5 rats receive the Standard Preparation and 5 rats receive the preparation being tested, and in which the mean responses are equal, the limits of error ($P = 0{\cdot}99$) are 65 and 154 per cent.

Q. *BIOLOGICAL ASSAY OF ANTISCORBUTIC VITAMIN (VITAMIN C)*

The activity of a preparation containing antiscorbutic vitamin (vitamin C) is determined by comparing its antiscorbutic activity with that of the Standard Preparation of Antiscorbutic Vitamin (Vitamin C) by a suitable method.

1. Standard Preparation of Antiscorbutic Vitamin (Vitamin C).

The Standard Preparation for Great Britain and Northern Ireland is a quantity of *l*-ascorbic acid kept in the National Institute for Medical Research, Hampstead, London. The Standard Preparation for other parts of the British Empire is the same, except for those countries in which a similar standard preparation, kept in a different institute, has been defined by law; in these countries the standard preparation, so defined, is used.

2. The Unit of Antiscorbutic Activity (Vitamin C).

The Unit of Antiscorbutic Activity (Vitamin C) for Great Britain and Northern Ireland is the same as the international unit. It is defined as the specific antiscorbutic activity contained in 0·05 milligram of the Standard Preparation. The Unit for other parts of the British Empire is the same, except for those countries in which a similar unit has been defined by law; in these countries the unit, so defined, is used.

3. Suggested Details of Method.

(*a*) *Changes in the histological structure of the teeth.*

When guinea-pigs are fed on diets deficient in vitamin C, changes are produced in the structure of their teeth. These changes are related to the degree of the deficiency and occur before other symptoms, such as tender gums and haemorrhages at the knee-joints.

Guinea-pigs, each weighing from 250 to 300 grammes, receive a basal diet free from vitamin C for fourteen days. A suitable diet consists of:—

Bran	45 per cent.
Split oats	25 per cent.
Dried skimmed milk . . .	30 per cent.

In addition each guinea-pig receives about 10 drops of a good sample of cod-liver oil twice a week and an unrestricted supply of fresh tap-water.

For the experiment two groups, each of 10 guinea-pigs, are used. Those in one group receive daily doses of the Standard Preparation, those in the other group receive daily doses of the preparation being tested, for fourteen days. A useful daily dose of the Standard Preparation is 1 milligram (20 Units). An amount of the preparation being tested which is expected to contain the equivalent of 1 milligram is given as a daily dose.

The guinea-pigs are killed, and the lower jaw-bones are removed and decalcified. Sections are cut of the root of the incisor at the region of the bend of the jaw-bone. They are stained with *solution of haematoxylin and alum*, followed by *solution of eosin*, or with *solution of haematoxylin and ferric ammonium sulphate*, followed by *solution of trinitrophenol and acid magenta*. The extent of disorganisation of the structure

is estimated by comparing the appearances with those shown in a graded series of sections derived from guinea-pigs, which have received different doses of the Standard Preparation with the same basal diet. The average degree of protection from scurvy of each group of guinea-pigs is determined. The degree of protection may be represented by the figures 0 to 4, a moderate degree of protection being represented by the figure 2·5. If the average degree of protection of the group, receiving the dose of the preparation being tested, is equal to that of the other group, simultaneously receiving the same dose of the Standard Preparation, the activity of the preparation is equal to that of the Standard Preparation. If the average degrees of protection of the two groups are not equal, and more exact information as to the activity of the preparation being tested is required, the test is repeated, using for one group of animals the same dose of the Standard Preparation and for the other group a dose of the preparation being tested, which, judging from the first test, is likely to produce a degree of protection equal to that produced by the dose of the Standard Preparation.

Limits of Error :—In an experiment in which the average effect (degree of protection from scurvy) is estimated for 10 guinea-pigs, the following statements can be made :—

(1) There is no conclusive evidence of the presence of vitamin C unless the effect is greater than 1·6.

(2) Two preparations can be shown to differ significantly in their activity only when their effects differ by more than 1 unit.

(3) When the effect of each preparation is 2·5, the limits of error (P = 0·99) are 36 and 164 per cent.

When the effect of each preparation is 3·0, the limits of error (P = 0·99) are 51 and 149 per cent.

(*b*) *Growth, and development of macroscopic lesions of scurvy.*

Young guinea-pigs, each weighing from 250 to 300 grammes, receive unrestricted quantities of a basal diet free from vitamin C. A suitable diet consists of :—

Wheat bran	.	.	.	6	parts by volume
Barley meal	.	.	.	2	,, ,, ,,
Wheat middlings	.	.	.	3	,, ,, ,,
Fish meal	.	.	.	1	,, ,, ,,
Crushed oats	.	.	.	4	,, ,, ,,

The whole is moistened with water. Each animal receives daily in addition 40 to 60 millilitres of milk, made up from a dried powder and autoclaved for fifteen minutes at 120°. On this diet, without addition of vitamin C in any form, guinea-pigs of the weight stipulated and derived from a good stock, which has received cabbage regularly, develop scurvy and die in four to five weeks.

In the experiment the doses are chosen with the aim of finding one dose of the preparation being tested, which produces a response equal to that given by a dose of the Standard Preparation. The average growth response to these doses should be subnormal, and the protection from scurvy should be only partial. Daily doses of 0·5 milligram and of 0·25 milligram of the Standard Preparation approximately conform to this requirement. Groups of 5 guinea-pigs, each receiving one of these amounts of the Standard Preparation, should be included in every comparison. Corresponding doses of the preparation being tested are given. A group of 5 animals is used for each dose of the preparation being tested.

In every group the daily dose is continued from the start of the experiment for not less than forty-two (and preferably for sixty) days, the animals being weighed twice a week throughout. The doses should be expeditiously consumed. At the end of the chosen period all the guinea-pigs are killed, and the signs of scurvy (hæmorrhages and fractures) are assessed. If the average growth and degree of protection from scurvy of the groups, receiving the doses of the preparation being tested, is equal or nearly equal to that of the other groups, receiving the same doses of the Standard Preparation, the activity of the preparation being tested is equal to that of the Standard Preparation. If the average degrees of protection of the respective groups are not equal or nearly equal, and more exact information as to the activity of the preparation being tested is required, the test is repeated, using fresh groups of guinea-pigs for the same dose of the Standard Preparation and other groups for doses of the preparation being tested, which, judging from the first test, are likely to produce a degree of protection equal to that produced by the doses of Standard Preparation.

Limits of Error :—In an experiment in which 10 guinea-pigs receive the Standard Preparation and 10 guinea-pigs receive the preparation being tested in a six weeks' test, and in which the dosage of each is just sufficient to maintain the

mean weight constant, the limits of error (P = 0·99) are 82 and 139 per cent. If the mean response is larger the error is also larger.

R. *BIOLOGICAL ASSAY OF ANTIPNEUMOCOCCUS SERUM (TYPE I)*

CAUTION.—In any part of the British Empire in which Antipneumococcus Serum (Type I) is controlled by law, care must be taken that the provisions of such law are duly complied with. (See British Pharmacopœia, 1932, page 12.)

The potency of a sample of antipneumococcus serum (type I) is determined by comparing the doses of it, necessary to protect mice against the lethal effect of *Diplococcus pneumoniæ (type I)*, with the doses of a standard preparation of antipneumococcus serum (type I), necessary to give the same protection. For this comparison there are necessary, (*a*) the Standard Preparation of Antipneumococcus Serum (Type I), and (*b*) a suspension of living, highly virulent *Diplococcus pneumoniæ (type I)*.

1. Standard Preparation of Antipneumococcus Serum (Type I).

The Standard Preparation for Great Britain and Northern Ireland is that defined in the Regulations made under the Therapeutic Substances Act, 1925. The Standard Preparation is a quantity of dried antipneumococcus serum (type I) kept in the National Institute for Medical Research, Hampstead, London. The Standard Preparation for other parts of the British Empire is the same, except for those countries in which a similar standard preparation, kept in a different institute, has been defined by law; in these countries the standard preparation, so defined, is used.

2. The Unit of Antipneumococcus Serum (Type I).

The Unit for Great Britain and Northern Ireland is that defined in the Regulations made under the Therapeutic Substances Act, 1925. The Unit is the specific neutralising activity for suitable cultures of *Diplococcus pneumoniæ (type I)*, contained in such an amount of the Standard Preparation as the Medical Research Council may from time to time indicate as the quantity exactly equivalent to the unit

accepted for international use. The Unit for other parts of the British Empire is the same, except for those countries in which a similar unit has been defined by law; in these countries the unit, so defined, is used.

3. Suggested Details of Method.

A. THE STRAIN OF *DIPLOCOCCUS PNEUMONIÆ* (*TYPE I*) USED IN THE TEST.

The strain used in the test possesses the morphological, biological and cultural characteristics of *Diplococcus pneumoniæ* (*type I*).

It is highly virulent for mice. The virulence is maintained by passage through mice at intervals of fourteen days to one month. For this purpose 0·5 millilitre of a suitable dilution of a young actively growing broth culture is injected intraperitoneally into mice. Cultures from the heart blood of these mice are inoculated into nutrient broth containing sterile blood. The strain is maintained in this medium at 0° to 4°.

B. PREPARATION OF THE CULTURE OF *DIPLOCOCCUS PNEUMONIÆ* (*TYPE I*) FOR USE IN THE TEST.

The culture of *Diplococcus pneumoniæ* (*type I*) for use in the test is prepared by adding 1 millilitre or less of the strain, maintained as described in the preceding paragraph, to approximately 10 millilitres of nutrient broth, to which 0·5 millilitre of sterile blood or serum may be added; the test culture is incubated at 37° for eighteen hours.

C. DETERMINATION OF THE POTENCY OF A SAMPLE OF ANTIPNEUMOCOCCUS SERUM (TYPE I).

(*a*) *By the method of intraperitoneal injection into mice of mixtures of the serum being tested and the test dose of the culture.*

The virulence of the strain is satisfactory, if not less than 2 out of 3 mice, injected intraperitoneally with 1×10^{-8} millilitre of the test culture, die within forty-eight hours.

In this method 1 volume of the test culture is added to 49 volumes of nutrient broth; 0·5 millilitre of the dilution, so obtained, contains the test dose of *Diplococcus pneumoniæ* (*type I*) for use in the tests.

The potency of a sample of antipneumococcus serum (type I) is determined by injecting into groups of mice mixtures

of graduated quantities of it and the test dose of the culture, and comparing the mortality rates with those produced by injecting, at the same time, into other groups of mice mixtures of known quantities of the Standard Preparation and the test dose of the culture. Graduated quantities of the serum being tested and of the Standard Preparation are chosen, the differences being such that mixtures, containing the larger quantities of serum being tested and of the Standard Preparation, may be expected to protect all, or nearly all, the mice injected, and that the smaller quantities of the serum being tested and of the Standard Preparation may be expected to protect few or none of the mice injected.

(1) *Preliminary Test.* Mixtures are made so that each millilitre of each mixture contains graduated quantities of the serum being tested together with the test dose of the culture; and mixtures are similarly made containing in each millilitre graduated quantities of the Standard Preparation together with the test dose of the culture. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride.* The mixtures are allowed to stand at room temperature for ten minutes.

One millilitre of each mixture is injected intraperitoneally into each of a group of 5 mice. The mice used are drawn from a uniform stock, and are preferably not less than 15 grammes, and not more than 20 grammes, in weight. The mice are thereafter observed for seven days. The relative protection conferred by the doses of the serum being tested, when compared with that given by the doses of the Standard Preparation, provides an approximate estimate of the potency of the sample of serum being tested.

(2) *Final Test.* Mixtures are made, containing in each millilitre graduated quantities of the serum being tested, and of the Standard Preparation, with the test dose of the culture. A number of mixtures containing the serum being tested, and a number of mixtures containing the Standard Preparation, are prepared, the quantities of the serum being tested and of the Standard Preparation being such as may be expected, from the results of the preliminary test, to confer on the mice in the various groups injected a high and a low degree of protection, as estimated by the mortality rates in each group. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride.* The mixtures are allowed to stand at room temperature for ten minutes.

A dose of 1 millilitre of each mixture is injected into each of a group of mice, not less than 100 mice in all being used for the serum being tested, and 100 mice in all for the Standard Preparation, under the same conditions as those described for the preliminary test. After seven days' observation the mortality rate for each group of mice is calculated.

The potency of the serum being tested is determined by comparison of the mortality rates in the groups of mice, which received doses of it, with the mortality rates in the groups of mice, which received the doses of the Standard Preparation.

Limits of Error :—If 100 mice receive the Standard Preparation and 100 mice receive the preparation being tested, the limits of error (P = 0·99) are 57 and 176 per cent.

(*b*) *By the method of intravenous injection into mice of the serum being tested, followed by the intraperitoneal injection of the test dose of the culture.*

In this method the test dose, appropriate for use in the determination of the potency of a sample of antipneumococcus serum (type I), is determined for each batch of medium which is reserved for the preparation of the test culture. The virulence of the test culture is such that a quantity not greater than 1×10^{-9} millilitre, when injected intraperitoneally in a volume of 1 millilitre, causes the death of not less than 5 of a group of 10 mice.

One Unit of the Standard Preparation, contained in 0·5 millilitre, is injected into a tail vein of each of 20 mice. One hour later each of a group of 10 of the mice is injected intraperitoneally with a dose of 0·001 millilitre of the test culture, contained in 0·5 millilitre, and each of the remaining 10 mice is injected intraperitoneally with a dose of 0·0005 millilitre of the culture, contained in 0·5 millilitre. At the same time 0·5 Unit of the Standard Preparation is injected into a tail vein of each of a group of 20 mice. One hour later each of a group of 10 of the mice is injected intraperitoneally with a dose of 0·001 millilitre of the test culture, contained in 0·5 millilitre, and each of the remaining 10 mice is injected intraperitoneally with a dose of 0·0005 millilitre of the culture, contained in 0·5 millilitre. The mice are observed for ninety-six hours. The appropriate test dose is estimated by noting the group of mice which gives a mortality rate most nearly approximating to 50 per cent.; the test dose, when the mortality rate is 50 per cent., contains 500,000–1,000,000

viable diplococci. The test dose of the culture in these tests is prepared by making the requisite dilutions in nutrient broth. The mice used are drawn from a uniform stock and are preferably not less than 18 grammes, and not more than 22 grammes, in weight.

(1) *Preliminary Test.* Graduated quantities of the serum being tested are given in a volume of 0·5 millilitre to groups of mice, each consisting of 10 animals ; the injection is made into a tail vein. At the same time a quantity of the Standard Preparation which is equivalent to 1 Unit, contained in a volume of 0·5 millilitre, is given to each of a group of 10 mice by injecting the dose into a tail vein. In the same way a quantity of the Standard Preparation which is equivalent to 0·5 Unit, contained in a volume of 0·5 millilitre, is injected into each of a group of 10 mice. One hour later the test dose of the culture, contained in a volume of 0·5 millilitre, is injected intraperitoneally into each mouse of all the groups. The animals are observed for ninety-six hours. The relative protection conferred by the doses of the serum being tested, as judged by the mortality rate in each group, when compared with that which is given by the doses of the Standard Preparation, provides an approximate estimate of the potency of the sample of serum being tested.

(2) *Final Test.* Three dilutions of the serum being tested are prepared in *physiological solution of sodium chloride* in accordance with the results of the preliminary test, so that each dose is contained in a volume of 0·5 millilitre. Dilutions of the Standard Preparation, which contain 1 Unit and 0·5 Unit in 0·5 millilitre, are also prepared in *physiological solution of sodium chloride*. A volume of 0·5 millilitre of each solution is injected into a tail vein of each of a group, consisting of not less than 20 mice. One hour later the test dose of the culture, contained in a volume of 0·5 millilitre, is injected intraperitoneally into each mouse of all of the groups. The animals are observed for ninety-six hours. The relative protection conferred by the doses of the serum being tested, as judged by the mortality rate in each group, when compared with that which is given by the doses of the Standard Preparation, provides an estimate of the potency of the sample of serum being tested.

Limits of Error :—If 20 mice are used in each of the five groups, the limits of error (P = 0·99) are 51 and 197 per cent.

S. *BIOLOGICAL ASSAY OF ANTIPNEUMOCOCCUS SERUM (TYPE II)*

CAUTION.—In any part of the British Empire in which Antipneumococcus Serum (Type II) is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

The biological assay of Antipneumococcus Serum (Type II) resembles that of Antipneumococcus Serum (Type I) with the modification that a suitable strain of *Diplococcus pneumoniæ* (*type II*) is used in the test.

T. *BIOLOGICAL ASSAY OF GAS-GANGRENE ANTITOXIN (ŒDEMATIENS)*

CAUTION.—In any part of the British Empire in which Gas-gangrene Antitoxin (œdematiens) is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

The potency of a sample of gas-gangrene antitoxin (œdematiens) is determined by comparing the dose of it, necessary to protect mice or other suitable animals against the toxic effects of gas-gangrene toxin (œdematiens), with the dose of a standard preparation of gas-gangrene antitoxin (œdematiens), necessary to give the same protection. For this comparison there are necessary, (*a*) the Standard Preparation of Gas-gangrene Antitoxin (œdematiens), and (*b*) a suitable preparation of gas-gangrene toxin (œdematiens) for use as a test toxin. The potency of this test toxin is first determined in relation to the Standard Preparation by a satisfactory method. The potency of samples of gas-gangrene antitoxin (œdematiens) to be tested is then determined in relation to the potency of the test toxin by the same method.

1. Standard Preparation of Gas-gangrene Antitoxin (œdematiens).

The Standard Preparation for Great Britain and Northern Ireland is that defined in the Regulations made under the Therapeutic Substances Act, 1925. The Standard Preparation is a quantity of dried gas-gangrene antitoxin (œdematiens) kept in the National Institute for Medical Research, Hampstead, London. The Standard Preparation for other parts of the British Empire is the same, except for those countries

in which a similar standard preparation, kept in a different institute, has been defined by law; in these countries the standard preparation, so defined, is used.

2. The Unit of Gas-gangrene Antitoxin (œdematiens).

The Unit for Great Britain and Northern Ireland is that defined in the Regulations made under the Therapeutic Substances Act, 1925. The Unit is the specific neutralising activity for gas-gangrene (œdematiens) toxin, contained in such an amount of the Standard Preparation as the Medical Research Council may from time to time indicate as the quantity exactly equivalent to the unit accepted for international use. The Unit for other parts of the British Empire is the same, except for those countries in which a similar unit has been defined by law; in these countries the unit, so defined, is used.

3. Suggested Details of Method.

A. Preparation of test toxin.

Gas-gangrene toxin (œdematiens) is prepared from a sterile filtrate of *Clostridium œdematiens*, the filtrate being prepared after about five days' growth of the organism, by precipitation with *ammonium sulphate*; the resulting precipitate is collected, dried in vacuo over *phosphorus pentoxide*, powdered, and kept dry.

B. Selection of test toxin.

A suitable toxin is one which is lethal for mice, when injected intramuscularly in a dose of 0·02 milligram, or less, and which has a test dose, as defined below, of 0·5 milligram, or less.

C. Determination of the test dose.

A quantity of the dried toxin is accurately weighed, and dissolved in *physiological solution of sodium chloride*, so that each millilitre contains a precise amount, such as 10 milligrams.

The Standard Preparation is issued as a solution in a mixture of 1 volume of *physiological solution of sodium chloride* and 2 volumes of *glycerin*; the solution contains 20 Units in 1 millilitre. This solution of the Standard Preparation is diluted with 99 volumes of *physiological solution of sodium chloride*, so that each millilitre contains 0·2 Unit.

(*a*) ***By intramuscular injection into mice.*** Mixtures are

made so that 0·2 millilitre of each mixture contains 0·1 millilitre of the dilution of the Standard Preparation (0·02 Unit) and a varying quantity of the solution of the toxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*.

The mixtures are allowed to stand at room temperature for sixty minutes, and are then injected into mice. The mice used are drawn from a uniform stock, and are preferably not less than 17 grammes, and not more than 20 grammes, in weight. A dose of 0·2 millilitre of each mixture is injected intramuscularly into each of 6 mice. The mice are thereafter observed for seventy-two hours.

If all the mice are killed, the amount of toxin present in 0·2 millilitre of the mixture is in excess of the test dose; if none of the mice is killed, the amount of toxin present in 0·2 millilitre of the mixture is less than the test dose. Fresh mixtures are made, containing in each 0·2 millilitre of each mixture 0·1 millilitre of the dilution of the Standard Preparation (0·02 Unit) and amounts of the solution of the toxin intermediate between the smallest amount which killed all the mice, and the largest amount which failed to kill any of the mice. The mixtures are allowed to stand at room temperature for sixty minutes. A dose of 0·2 millilitre of each mixture is injected intramuscularly into each of 6 mice. The mice are thereafter observed for seventy-two hours. The determination is repeated, and the results of the separate tests which have been made with mixtures of the same composition are added together, so that a series of totals is obtained, each total representing the mortality due to one mixture.

The test dose of toxin is the amount present in 0·2 millilitre of that mixture which causes the death of about one-half of the total number of mice injected with it.

(*b*) *By intracutaneous injection into guinea-pigs.* The mixtures of toxin and the dilution of the Standard Preparation, for the determination of the test dose of the toxin by intracutaneous injection into guinea-pigs, are prepared in a manner identical with that described for the determination of the test dose by the intramuscular injection into mice.

The mixtures are allowed to stand at room temperature for sixty minutes, and are then injected intracutaneously into the shaven or depilated flanks of white or light-coloured guinea-pigs, each weighing from 300 to 400 grammes. A

dose of 0·2 millilitre of each mixture is injected at suitably spaced intervals into the skin of the guinea-pig. The guinea-pigs are thereafter observed for seven days.

The test dose of the toxin is the amount present in 0·2 millilitre of that mixture which causes at the site of injection a small, characteristic, œdematous, and eventually necrotic, lesion in the skin of the guinea-pig. Mixtures containing larger amounts of toxin cause a greater amount of œdema and necrosis, and mixtures containing smaller amounts of toxin cause no reaction.

D. DETERMINATION OF THE POTENCY OF A SAMPLE OF ANTITOXIN.

(*a*) *By intramuscular injection into mice.*

(1) *Preliminary Test.* A quantity of the test toxin is accurately weighed, and dissolved in *physiological solution of sodium chloride*, so that 0·1 millilitre contains the test dose.

Mixtures are made so that 0·2 millilitre of each mixture contains 0·1 millilitre of the solution of the toxin and different quantities of the antitoxin being tested. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*. The mixtures are allowed to stand at room temperature for sixty minutes. A dose of 0·2 millilitre of each mixture is injected into each of 3 mice under the conditions described in the determination of the test dose of toxin. If none of the mice is killed, 0·2 millilitre of the mixture contains more than 0·02 Unit of Antitoxin ; similarly, if all the mice are killed, 0·2 millilitre of the mixture contains less than 0·02 Unit of Antitoxin.

(2) *Final Test.* Fresh mixtures are made, containing in each 0·2 millilitre the test dose of toxin and amounts of the antitoxin being tested intermediate between the smallest amount of antitoxin which protects all the mice, and the largest amount of antitoxin which fails to protect any of the mice, as determined in the preliminary test.

A further mixture is made with the dilution of the Standard Preparation such that 0·2 millilitre contains 0·1 millilitre of the solution of the toxin and 0·02 Unit of Antitoxin.

The mixtures are allowed to stand at room temperature for exactly sixty minutes. A dose of 0·2 millilitre of each mixture is injected into each of 6 mice under the conditions described in the determination of the test dose.

The mixture of the antitoxin being tested, which contains 0·02 Unit in 0·2 millilitre, is that mixture which, killing some but not all of the mice, kills the same, or most nearly the same, number as the mixture, containing 0·02 Unit of Antitoxin in 0·2 millilitre.

Limits of Error :—The limits of error (P = 0·99) are 95 and 105 per cent.

(*b*) *By intracutaneous injection into guinea-pigs.*

A quantity of the test toxin is accurately weighed, and dissolved in *physiological solution of sodium chloride*, so that 0·1 millilitre contains the test dose.

Mixtures are made so that 0·2 millilitre of each mixture contains 0·1 millilitre of the solution of the toxin and different volumes of the antitoxin being tested.

A further mixture is made with the dilution of the Standard Preparation such that each 0·2 millilitre contains 0·1 millilitre of the solution of toxin and 0·02 Unit of Antitoxin.

The mixtures are allowed to stand at room temperature for sixty minutes. A dose of 0·2 millilitre of each mixture is injected into each of 2 guinea-pigs under the conditions described in the determination of the test dose of toxin.

The mixture of antitoxin being tested, which contains 0·02 Unit in 0·2 millilitre, is that mixture which produces the same degree of local reaction as that produced by the injection of the mixture, which contains in 0·2 millilitre the test dose of toxin and 0·02 Unit of Antitoxin.

Limits of Error:—The data at present available do not permit of a sufficiently accurate determination of the limits of error, but the limits are not greatly wider than the limits of error for the test by intramuscular injection into mice.

U. *BIOLOGICAL ASSAY OF GAS-GANGRENE ANTITOXIN (VIBRION SEPTIQUE)*

CAUTION.—In any part of the British Empire in which Gas-gangrene Antitoxin (vibrion septique) is controlled by law, care must be taken that the provisions of such law are duly complied with. (*See British Pharmacopœia, 1932, page 12.*)

The potency of a sample of gas-gangrene antitoxin (vibrion septique) is determined by comparing the dose of it, necessary to protect mice or other suitable animals against the toxic effects of gas-gangrene toxin (vibrion septique), with the dose of a standard preparation of gas-gangrene antitoxin (vibrion

septique), necessary to give the same protection. For this comparison there are necessary, (*a*) the Standard Preparation of Gas-gangrene Antitoxin (vibrion septique), and (*b*) a suitable preparation of gas-gangrene toxin (vibrion septique) for use as a test toxin. The potency of this test toxin is first determined in relation to the Standard Preparation by a satisfactory method. The potency of samples of gas-gangrene antitoxin (vibrion septique) to be tested is then determined in relation to the potency of the test toxin by the same method.

1. Standard Preparation of Gas-gangrene Antitoxin (vibrion septique).

The Standard Preparation for Great Britain and Northern Ireland is that defined in the Regulations made under the Therapeutic Substances Act, 1925. The Standard Preparation is a quantity of dried gas-gangrene antitoxin (vibrion septique) kept in the National Institute for Medical Research, Hampstead, London. The Standard Preparation for other parts of the British Empire is the same, except for those countries in which a similar standard preparation, kept in a different institute, has been defined by law; in these countries the standard preparation, so defined, is used.

2. The Unit of Gas-gangrene Antitoxin (vibrion septique).

The Unit for Great Britain and Northern Ireland is that defined in the Regulations made under the Therapeutic Substances Act, 1925. The Unit is the specific neutralising activity for gas-gangrene (vibrion septique) toxin, contained in such an amount of the Standard Preparation as the Medical Research Council may from time to time indicate as the quantity exactly equivalent to the unit accepted for international use. The Unit for other parts of the British Empire is the same, except for those countries in which a similar unit has been defined by law; in these countries the unit, so defined, is used.

3. Suggested Details of Method.

A. Preparation of test toxin.

Gas-gangrene toxin (vibrion septique) is prepared from a sterile filtrate of the *Clostridium*, commonly known as Vibrion Septique, the filtrate being prepared after one to three days' growth of the organism, by precipitation with *ammonium*

sulphate; the resulting precipitate is collected, dried in vacuo over *phosphorus pentoxide*, powdered, and kept dry.

B. SELECTION OF TEST TOXIN.

A suitable toxin is one which is lethal for mice, when injected intravenously in a dose of 0·2 milligram, or less, and which has a test dose, as defined below, of 5·0 milligrams, or less.

C. DETERMINATION OF THE TEST DOSE.

A quantity of the dried toxin is accurately weighed, and dissolved in *physiological solution of sodium chloride*, so that each millilitre contains a precise amount, such as 20 milligrams.

The Standard Preparation is issued as a solution in a mixture of 1 volume of *physiological solution of sodium chloride* and 2 volumes of *glycerin*; the solution contains 100 Units in 1 millilitre. This solution of the Standard Preparation is diluted with 19 volumes of *physiological solution of sodium chloride*, so that each millilitre contains 5 Units.

(*a*) *By intravenous injection into mice.*

Mixtures are made so that 0·5 millilitre of each mixture contains 0·2 millilitre of the dilution of the Standard Preparation (1 Unit) and a varying quantity of the solution of the toxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*.

The mixtures are allowed to stand at room temperature for sixty minutes, and are then injected into mice. The mice used are drawn from a uniform stock, and are preferably not less than 17 grammes, and not more than 20 grammes, in weight. A dose of 0·5 millilitre of each mixture is injected into a tail vein of each of 6 mice. The mice are thereafter observed for seventy-two hours.

The test dose of toxin is the amount present in 0·5 millilitre of that mixture which causes the death of some of the mice but not of all of them, provided that mixtures, containing larger amounts of toxin, cause the death of all the mice injected, and that mixtures, containing smaller amounts of toxin, fail to kill any of the mice injected.

(*b*) *By intracutaneous injection into guinea-pigs.*

Mixtures are made so that 0·2 millilitre of each mixture contains 0·1 millilitre of the dilution of the Standard Pre-

paration (0·5 Unit) and a varying quantity of the solution of the toxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride.*

The mixtures are allowed to stand at room temperature for sixty minutes, and are then injected intracutaneously into the shaven or depilated flanks of white or light-coloured guinea-pigs, each weighing from 300 to 400 grammes. A dose of 0·2 millilitre of each mixture is injected at suitably spaced intervals into the skin of the guinea-pig. The guinea-pigs are thereafter observed for forty-eight hours.

The test dose of the toxin is the amount present in 0·2 millilitre of that mixture which causes at the site of injection a small, characteristic, necrotic lesion in the skin of the guinea-pig. Mixtures containing larger amounts of toxin cause a greater amount of œdema and necrosis, and mixtures containing smaller amounts of toxin cause no reaction.

D. DETERMINATION OF THE POTENCY OF A SAMPLE OF ANTITOXIN.

(*a*) *By intravenous injection into mice.*

(1) *Preliminary Test.* A quantity of the test toxin is accurately weighed, and dissolved in *physiological solution of sodium chloride*, so that 0·2 millilitre contains the test dose.

Mixtures are made so that 0·5 millilitre of each mixture contains 0·2 millilitre of the solution of toxin and different quantities of the antitoxin being tested. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride.* The mixtures are allowed to stand at room temperature for sixty minutes. A dose of 0·5 millilitre of each mixture is injected into each of 3 mice under the conditions described in the determination of the test dose of toxin. If none of the mice is killed, 0·5 millilitre of the mixture contains more than 1 Unit of Antitoxin; similarly, if all the mice are killed, 0·5 millilitre of the mixture contains less than 1 Unit of Antitoxin.

(2) *Final Test.* Fresh mixtures are made, containing in each 0·5 millilitre the test dose of toxin and amounts of the antitoxin being tested intermediate between the smallest amount of antitoxin, protecting all the mice, and the largest amount of antitoxin, failing to protect any of the mice, as determined in the preliminary test.

A further mixture is made with the dilution of the Standard

Preparation such that 0·5 millilitre contains 0·2 millilitre of the toxin solution and 1 Unit of Antitoxin.

The mixtures are allowed to stand at room temperature for sixty minutes. A dose of 0·5 millilitre of each mixture is injected into each of 6 mice under the conditions described in the determination of the test dose.

The mixture of the antitoxin being tested, which contains 1 Unit in 0·5 millilitre, is that mixture which, killing some but not all of the mice, kills the same, or most nearly the same, number as the mixture, which contains 1 Unit of Antitoxin in 0·5 millilitre.

Limits of Error :—The limits of error (P = 0·99) are 89 and 111 per cent.

(*b*) *By intracutaneous injection into guinea-pigs.*

A quantity of the test toxin is accurately weighed, and dissolved in *physiological solution of sodium chloride*, so that 0·1 millilitre contains the test dose.

Mixtures are made so that 0·2 millilitre of each mixture contains 0·1 millilitre of the solution of the toxin and different quantities of the antitoxin being tested.

A further mixture is made with the dilution of the Standard Preparation such that each 0·2 millilitre contains 0·1 millilitre of the solution of toxin and 0·5 Unit of Antitoxin.

The mixtures are allowed to stand at room temperature for sixty minutes. A dose of 0·2 millilitre of each mixture is injected into each of 2 guinea-pigs under the conditions described in the determination of the test dose of toxin.

The mixture of antitoxin being tested, which contains 0·5 Unit in 0·2 millilitre, is that mixture which produces the same degree of local reaction as that produced by the injection of the mixture which contains in 0·2 millilitre the test dose of toxin and 0·5 Unit of Antitoxin.

Limits of Error :—The data at present available do not permit of a sufficiently accurate determination of the limits of error, but the limits are certainly not wider than the limits of error for the test by intravenous injection into mice.

V. *BIOLOGICAL ASSAY OF STAPHYLOCOCCUS ANTITOXIN*

CAUTION.—In any part of the British Empire in which Staphylococcus Antitoxin is controlled by law, care must be taken that the provisions of such law are duly complied with. (See British Pharmacopœia, 1932, page 12.)

The potency of a sample of staphylococcus antitoxin is determined by comparing the dose of it, necessary to neutralise the specific haemolytic, dermo-necrotic or lethal effects of staphylococcus toxin, with the dose of a standard preparation of staphylococcus antitoxin, necessary to give the same protection. For this comparison there are necessary, (*a*) the Standard Preparation of Staphylococcus Antitoxin, and (*b*) a suitable preparation of staphylococcus toxin for use as a test toxin. The potency of this test toxin is first determined in relation to the Standard Preparation by a satisfactory method. The potency of samples of staphylococcus antitoxin to be tested is then determined in relation to the potency of the test toxin by the same method.

1. Standard Preparation of Staphylococcus Antitoxin.

The Standard Preparation for Great Britain and Northern Ireland is that defined under the Therapeutic Substances Act, 1925. The Standard Preparation is a quantity of dried staphylococcus antitoxin kept in the National Institute for Medical Research, Hampstead, London. The Standard Preparation for other parts of the British Empire is the same, except for those countries in which a similar standard preparation, kept in a different institute, has been defined by law; in these countries the standard preparation, so defined, is used.

2. The Unit of Staphylococcus Antitoxin.

The Unit for Great Britain and Northern Ireland is that defined in the Regulations made under the Therapeutic Substances Act, 1925. The Unit is the specific neutralising activity for staphylococcus toxin, contained in such an amount of the Standard Preparation as the Medical Research Council may from time to time indicate as the quantity exactly equivalent to the unit accepted for international use. The Unit for other parts of the British Empire is the same, except for those countries in which a similar unit has been defined by law; in these countries the unit, so defined, is used.

3. Suggested Details of Method.

A. PREPARATION OF TEST TOXIN.

Staphylococcus toxin is prepared by separating the fluid portion from the growth of a toxigenic strain of *Staphylococcus* on a fluid or semifluid medium, or by extraction of the organisms or of the medium on which the organisms have been grown. It is sterilised by *filtration*.

B. SELECTION OF TEST TOXIN.

In selecting a toxin for use as a test toxin the following quantities of the sample are determined :—

(i) *the LH dose.* This is the smallest quantity of the toxin which, when mixed with 1 Unit of Antitoxin, causes partial haemolysis of a rabbit's washed red blood corpuscles, which have been added as indicator.

(ii) *the Lr/5 dose.* This is the smallest quantity of toxin which, when mixed with one-fifth of a Unit of Antitoxin, and injected into the skin of a normal guinea-pig or rabbit, causes a small, characteristic, necrotic lesion at the site of injection.

(iii) *the L_t dose.* This is the smallest quantity of the toxin which, when mixed with 1 Unit of Antitoxin and injected intravenously or intraperitoneally into mice, causes the death within three days of about one-half of the mice injected.

A suitable toxin is one which (*a*) causes the haemolysis of washed red blood corpuscles of the rabbit in doses of 0·005 millilitre, or less, and which has a test dose (LH) of 0·3 millilitre, or less ; (*b*) produces a small, characteristic, necrotic lesion in guinea-pigs when injected intracutaneously in doses of 0·01 millilitre, or less, and which has a test dose (Lr/5) of 0·1 millilitre, or less ; (*c*) produces a small, characteristic, necrotic lesion in rabbits when injected intracutaneously in doses of 0·002 millilitre, or less, and which has a test dose (Lr/5) of 0·05 millilitre, or less ; (*d*) is lethal for mice when injected intravenously or intraperitoneally in doses of 0·05 millilitre or less, and has a test dose (L_t) of 0·3 millilitre, or less.

C. DETERMINATION OF THE TEST DOSE.

The Standard Preparation is issued as a solution in a mixture of 1 volume of *physiological solution of sodium chloride* and 2 volumes of *glycerin* ; the solution contains 20 Units in 1 millilitre.

(*a*) *By the haemolysis of washed red blood corpuscles of the rabbit.*

One volume of the solution of the Standard Preparation is diluted with 19 volumes of *physiological solution of sodium chloride*, or other appropriate saline solution, so that each millilitre contains 1 Unit.

Mixtures are made so that 2 millilitres of each mixture contains 1 millilitre of the dilution of the Standard Preparation (1 Unit) and a varying quantity of the solution of the toxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*, or other appropriate saline solution.

The mixtures are allowed to stand at room temperature for thirty minutes; 0·5 millilitre of a 2 per cent. suspension of washed red blood corpuscles of the rabbit is then added to 2 millilitres of each mixture, and the mixtures are incubated at 37° for sixty minutes. The mixtures are thereafter placed at room temperature, and are examined after one hour, or after a period not exceeding twenty-four hours.

The test dose (LH) of the toxin is the amount present in 2 millilitres of that mixture which causes partial haemolysis of the red blood corpuscles added as indicator.

(*b*) *By intracutaneous injection into guinea-pigs.*

One volume of the solution of the Standard Preparation is diluted with 9 volumes of *physiological solution of sodium chloride*, or other appropriate saline solution, so that each millilitre contains 2 Units.

Mixtures are made so that 2 millilitres of each mixture contains 1 millilitre of the dilution of the Standard Preparation (2 Units) and a varying quantity of the solution of the toxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*, or other appropriate saline solution.

The mixtures are allowed to stand at room temperature for thirty minutes, and are then injected intracutaneously into the shaven or depilated flanks of not less than 2 white or light-coloured guinea-pigs, preferably weighing not less than 300 grammes. A dose of 0·2 millilitre of each mixture is injected at suitably spaced intervals into the skin of the guinea-pig; not more than five injections are made into one flank. The guinea-pigs are thereafter observed for two days.

The test dose (Lr/5) of the toxin is the amount present in 0·2 millilitre of that mixture which causes at the site of injection a small, characteristic, necrotic lesion in the skin of the guinea-pig. Mixtures containing larger amounts of toxin cause a greater amount of necrosis and inflammation, and mixtures containing smaller amounts of toxin cause no necrosis.

(*c*) *By intracutaneous injection into rabbits.*

The method is the same as that described in the preceding paragraph (C (*b*)) except that 0·2 millilitre of each mixture is injected into the shaven or depilated skin of rabbits. The rabbits are thereafter observed for four days.

The test dose (Lr/5) of the toxin is the amount present in 0·2 millilitre of that mixture which causes at the site of injection a small, characteristic, necrotic lesion in the skin of the rabbit. Mixtures containing larger quantities of toxin cause a greater amount of necrosis and inflammation, and mixtures containing smaller amounts of toxin cause no necrosis.

NOTE.—By employing larger or smaller quantities of the Standard Preparation in the mixtures, prepared for the methods based upon the intracutaneous tests in guinea-pigs (paragraph C (*b*)) or rabbits (paragraph C (*c*)), the test dose of the toxin determined against one-half (Lr/2) or one-tenth (Lr/10) of a Unit of Antitoxin may be similarly determined.

(*d*) *By intravenous injection into mice.*

The Standard Preparation is used. Mixtures are made so that 0·5 millilitre of each mixture contains 0·05 millilitre of the Standard Preparation (1 Unit) and a varying quantity of the solution of the toxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*, or other appropriate saline solution.

The mixtures are allowed to stand at room temperature for thirty minutes, and are then injected into mice. The mice used are drawn from a uniform stock and are preferably not less than 17 grammes, and not more than 22 grammes, in weight. For each mixture a group of 6 mice is selected, and 0·5 millilitre of the mixture is injected into a tail vein of each mouse. The mice are thereafter observed for three days.

The determination is repeated ; and the results of the separate tests, which have been made with mixtures of the same composition, are added together so that a series of totals is obtained, each total representing the mortality due to one mixture.

The test dose (L_t) of the toxin is the amount present in 0·5 millilitre of that mixture which causes the death of about one-half of the total number of mice injected with it.

(*e*) *By intraperitoneal injection into mice.*

The method is the same as that described in the preceding paragraph (C (*d*)) except that the mice used for the determination are injected intraperitoneally.

D. DETERMINATION OF THE POTENCY OF A SAMPLE OF ANTITOXIN.

(*a*) *By the haemolysis of washed red blood corpuscles of the rabbit.*

The test toxin is diluted with *physiological solution of sodium chloride*, or other appropriate saline solution, so that 1 millilitre of the dilution contains the test dose (LH).

Mixtures are made so that 2 millilitres of each mixture contains 1 millilitre of the dilution of the toxin and different quantities of the antitoxin being tested. A further mixture is made with the dilution of the Standard Preparation so that 2 millilitres contains 1 millilitre of the dilution of toxin and 1 Unit of Antitoxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*, or other appropriate saline solution. The mixtures are allowed to stand at room temperature for thirty minutes ; 0·5 millilitre of a 2 per cent. suspension of washed red blood corpuscles of the rabbit is added to 2 millilitres of each mixture. The mixtures are incubated at 37° for sixty minutes under the conditions described in the determination of the test dose (LH).

The mixture of the antitoxin being tested, which contains 1 Unit in 2 millilitres, is that mixture which shows the same, or most nearly the same, amount of partial hæmolysis as is shown by the mixture which contains the test dose of toxin and 1 Unit of Antitoxin.

Limits of Error :—The limits of error (P = 0·99) are 89·5 and 110·5 per cent.

(*b*) *By intracutaneous injection into guinea-pigs.*

The test toxin is diluted with *physiological solution of sodium chloride*, or other appropriate saline solution, so that 1 millilitre of the dilution contains ten times the test dose (Lr/5).

Mixtures are made so that 2 millilitres of each mixture contains 1 millilitre of the dilution of toxin and different quantities of the antitoxin being tested. A further mixture is made so that 2 millilitres contains 1 millilitre of the dilution of toxin and 2 Units of Antitoxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*, or other appropriate saline solution.

The mixtures are allowed to stand at room temperature for thirty minutes. A dose of 0·2 millilitre of each mixture is injected into each of 2 guinea-pigs under the conditions described in the determination of the test dose (Lr/5) of toxin.

The mixture of the antitoxin being tested, which contains 0·2 Unit in 0·2 millilitre, is that mixture which produces the same degree of necrosis as that produced by the injection into the same animal of the mixture which contains in 0·2 millilitre the test dose (Lr/5) of the toxin and 0·2 Unit of Antitoxin.

Limits of Error :—The limits of error (P = 0·99) are 86 and 114 per cent.

(*c*) *By intracutaneous injection into rabbits.*

The method is the same as that described in the preceding paragraph (D (*b*)) except that 0·2 millilitre of each mixture is injected into rabbits under the conditions described in the determination of the test dose (Lr/5).

Limits of Error :—The data at present available do not permit of a sufficiently accurate determination of the limits of error, but the limits are not wider than the limits of error for the test by intracutaneous injection into guinea-pigs.

(*d*) *By intravenous injection into mice.*

Mixtures are made so that 0·5 millilitre of each mixture contains the test dose (L_t) of the toxin and different quantities of the antitoxin being tested. A further mixture is made so that 0·5 millilitre contains the test dose of the toxin and

1 Unit of Antitoxin. The total volume of each mixture is adjusted by dilution with *physiological solution of sodium chloride*, or other appropriate saline solution.

The mixtures are allowed to stand at room temperature for thirty minutes. For each mixture a group of 6 mice is selected, and 0·5 millilitre of the mixture is injected into a tail vein of each mouse. The mice are thereafter observed for three days.

The mixture of the antitoxin being tested, which contains 1 Unit in 0·5 millilitre, is that mixture, killing some but not all of the mice, which kills the same, or most nearly the same, number as the mixture which contains in 0·5 millilitre the test dose (L_t) of the toxin and 1 Unit of Antitoxin.

Limits of Error :—If the preparation being tested is given in doses differing by 10 per cent. to groups of 6 mice, and if the Standard Preparation is given to 6 mice, the limits of error (P = 0·99) are 92 and 108 per cent.

(*e*) *By intraperitoneal injection into mice.*

The method is the same as that described in the preceding paragraph (D (*d*)) except that the mice used for the determination are injected intraperitoneally.

Limits of Error :—If the preparation being tested is given in doses differing by 10 per cent. to groups of 6 mice, and if the Standard Preparation is given to 6 mice, the limits of error (P = 0·99) are 87 and 115 per cent.

APPENDIX XVI

A. *METHODS OF STERILISING SOLUTIONS FOR INJECTION*

Page 631,

delete lines 5 and 6 ;

insert " A solution to be sterilised by Tyndallisation is prepared by aseptic methods and distributed in sterilised containers, which are then sealed and heated,".

C. *TESTS FOR LIMIT OF ALKALINITY OF GLASS*

Page 634,

delete lines 27–31;

insert "**Strong Solution of Methyl Red**: dissolve 0·04 gramme of *methyl red* in 75 millilitres of *alcohol (95 per cent.)*; add 1·5 millilitres of *N/20 sodium hydroxide*, or a quantity sufficient to adjust the solution so that the colour corresponds to about *p*H 5·2, and dilute with *water* to 100 millilitres.".

APPENDIX XXI

WEIGHTS AND MEASURES OF THE BRITISH PHARMACOPŒIA

Page 639, after line 11,

insert "1 microgram (γ) = The 1000th part of 1 milligram".

after line 25,

insert "1 Millimicron ($m\mu$) = the 1000th part of 1 micron".

INDEX

The Index is arranged according to the alphabetical order of the English names of the official drugs and preparations. The Latin names of the official drugs and preparations, with the exception of Synonyms, are not included in the Index, because the text of the Addendum, like that of the Pharmacopœia, is arranged according to the alphabetical order of the Latin names.

Hydroxides, oxides and salts occurring only in the Appendices are indexed under the names of their metals.

Synonyms appear with cross references.

Italic figures refer to the Appendices.

	PAGE
Acacia, Injection of Sodium Chloride and	39
Acetarsol	3
Acetarsone, *see* Acetarsol	3
Acetate—	
Lead	55
Acid Magenta	77
Acid Magenta and Trinitrophenol, Solution of	*78*
Acids—	
Acid, Arsanilic	*75*
Acid, Arsanilic, Solution of	*75*
Acid, Ascorbic	4
Acid, Formic	*76*
Acid, Picrolonic	*77*
Acid, Sulphanilic	*78*
Acid, Sulphuric (50 per cent. v/v)	*78*
Acriflavine	6
Additions	xxiv
Adrenaline	8
Adrenaline Hydrochloride, Solution of	42
Adsorbate of Vitamin B_1	57
Alkalinity of Glass, Tests for Limit of	*118*
Aloin	8
Alum	8
Alum and Hæmatoxylin, Solution of	*76*
Amended Monographs	xxiv
Antineuritic Vitamin (Vitamin B_1), Biological Assay of	*91*
Antipneumococcus Serum (Type I)	60
Antipneumococcus Serum (Type I), Biological Assay of	*97*
Antipneumococcus Serum (Type II)	61
Antipneumococcus Serum (Type II), Biological Assay of	*102*
Antirachitic Vitamin (Vitamin D), Biological Assay of	*84*
Antiscorbutic Vitamin (Vitamin C), Biological Assay of	*93*
Antitoxin, Gas-gangrene (œdematiens)	9

PAGE
Antitoxin, Gas-gangrene (œdematiens), Biological Assay of . *102*
Antitoxin, Gas-gangrene (perfringens), Biological Assay of . *86*
Antitoxin, Gas-gangrene (vibrion septique) . . . 12
Antitoxin, Gas-gangrene (vibrion septique), Biological Assay of *106*
Antitoxin, Staphylococcus 11
Antitoxin, Staphylococcus, Biological Assay of . . . *111*
Aqueous Solution of Iodine 44
Arachis Oil *75*
Argentum-Proteinicum Forte, *see* Argentoproteinum . . 15
Arsanilic Acid *75*
Arsanilic Acid, Solution of *75*
Arsenic, Quantitative Test for *82*
Ascorbic Acid 4
Assay of Vitamin A *86*
1. Standard Preparation *86*
2. The Unit *87*
3. Suggested Details of Biological Method . . . *87*
(*a*) Increase in weight in rats which have ceased to grow on a diet deficient in vitamin A . *87*
Limits of error *89*
(*b*) Prophylactic *89*
Limits of error *89*
4. Suggested Details of Spectrophotometric Method . *89*
Preparation of the solution of the unsaponifiable matter *90*
Limits of error *90*
Assays, Biological—
Assay, Biological, of Antineuritic Vitamin (Vitamin B_1) *91*
Assay, Biological, of Antiscorbutic Vitamin (Vitamin C) *93*
Assay, Biological, of Antirachitic Vitamin (Vitamin D) *84*
Assay, Biological, of Antipneumococcus Serum (Type I) *97*
Assay, Biological, of Antipneumococcus Serum (Type II) *102*
Assay, Biological, of Gas-gangrene Antitoxin (œdematiens) *102*
Assay, Biological, of Gas-gangrene Antitoxin (perfringens) *86*
Assay, Biological, of Gas-gangrene Antitoxin (vibrion septique) *106*
Assay, Biological, of Powdered Digitalis *86*
Assay, Biological, of Staphylococcus Antitoxin . . *111*
Atropine Sulphate 16
Australian Committee on Pharmacopœia Revision, Introduction xix

Barium Hydroxide, Solution of, N/10 . . . . *78*
Beeswax, Yellow 25
Belladonna Leaf 16
Belladonna, Liniment of 42
Belladonna, Liquid Extract of 29
Bicarbonate—
Potassium 55

PAGE

Biological Assays—
Biological Assay of Antineuritic Vitamin (Vitamin B_1) *91*
1. Standard Preparation *91*
2. The Unit *91*
3. Suggested Details of Method *91*
Limits of error *93*
Biological Assay of Antipneumococcus Serum (Type I) *97*
1. Standard Preparation *97*
2. The Unit *97*
3. Suggested Details of Method *98*
A. The strain of *Diplococcus pneumoniæ* (*type I*) used in the test *98*
B. Preparation of the culture of *Diplococcus pneumoniæ* (*type I*) for use in the test *98*
C. Determination of the potency of a sample of antipneumococcus serum (type I). *98*
(*a*) By the method of intraperitoneal injection into mice of mixtures of the serum being tested and the test dose of the culture . . . *98*
Limits of error *100*
(*b*) By the method of intravenous injection into mice of the serum being tested, followed by the intraperitoneal injection of the test dose of the culture *100*
Limits of error *101*
Biological Assay of Antipneumococcus Serum (Type II) *102*
Biological Assay of Antirachitic Vitamin (Vitamin D) . *84*
Biological Assay of Antiscorbutic Vitamin (Vitamin C) *93*
1. Standard Preparation *93*
2. The Unit *94*
3. Suggested Details of Method *94*
(*a*) Changes in the histological structure of the teeth *94*
Limits of error *95*
(*b*) Growth, and development of macroscopic lesions of scurvy *95*
Limits of error *96*
Biological Assay of Gas-gangrene Antitoxin (œdematiens) *102*
1. Standard Preparation *102*
2. The Unit *103*
3. Suggested Details of Method *103*
A. Preparation of Test Toxin *103*
B. Selection of Test Toxin *103*
C. Determination of the Test Dose . . *103*
(*a*) By intramuscular injection into mice *103*
(*b*) By intracutaneous injection into guinea-pigs *104*

Biological Assays (*continued*)— PAGE
Gas-Gangrene Antitoxin (œdematiens), Suggested Details of Method (*continued*)—
D. Determination of the potency of a sample of antitoxin 105
(*a*) By intramuscular injection into mice . 105
Limits of error 106
(*b*) By intracutaneous injection into guinea-pigs 106
Limits of error 106
Biological Assay of Gas-gangrene Antitoxin (perfringens) 86
Biological Assay of Gas-gangrene Antitoxin (vibrion septique) 106
1. Standard Preparation 107
2. The Unit 107
3. Suggested Details of Method 107
A. Preparation of Test Toxin 107
B. Selection of Test Toxin 108
C. Determination of the Test Dose . . 108
(*a*) By intravenous injection into mice. 108
(*b*) By intracutaneous injection into guinea-pigs 108
D. Determination of the potency of a sample of antitoxin 109
(*a*) By intravenous injection into mice. 109
Limits of error 110
(*b*) By intracutaneous injection into guinea-pigs 110
Limits of error 110
Biological Assay of Powdered Digitalis . . . 86
Biological Assay of Staphylococcus Antitoxin . . 111
1. Standard Preparation 111
2. The Unit 111
3. Suggested Details of Method 112
A. Preparation of Test Toxin . . . 112
B. Selection of Test Toxin 112
(i) the LH dose 112
(ii) the Lr/5 dose 112
(iii) the L_f dose 112
C. Determination of the Test Dose . . 112
(*a*) By the haemolysis of washed red blood corpuscles of the rabbit . . 113
(*b*) By intracutaneous injection into guinea-pigs 113
(*c*) By intracutaneous injection into rabbits 114
(*d*) By intravenous injection into mice. 114
(*e*) By intraperitoneal injection into mice 115
D. Determination of the potency of a sample of antitoxin 115
(*a*) By the haemolysis of washed red blood corpuscles of the rabbit . 115
Limits of error 115

Biological Assays (*continued*)— PAGE
Staphylococcus Antitoxin, Determination of the potency of a sample of antitoxin (*continued*)—
(*b*) By intracutaneous injection into guinea-pigs *116*
Limits of error *116*
(*c*) By intracutaneous injection into rabbits *116*
Limits of error *116*
(*d*) By intravenous injection into mice. *116*
Limits of error *117*
(*e*) By intraperitoneal injection into mice *117*
Limits of error *117*
Biological Assays, Errors of, General Notices . . . 1
Biological Products Committee, Introduction . . . xii
Bismuth, Injection of 37
Bismuth, Precipitated 19
Bismuth Carbonate 17
Bismuth Oxychloride 18
Bismuth Oxychloride, Injection of 38
Bismuth Salicylate, Injection of 38
Bismuth Sodium Tartrate, *see* Bismuthi et Sodii Tartras . 17
Bismuth Subchloride, *see* Bismuthi Oxychloridum . . 18
Bismuthyltartrate—
Sodium 17
Bisulphate—
Quinine *77*
British Pharmacopœia Commission ix
British Pharmacopœia Commission, Appointment of, Preface vii
Buchu 19

Cajuput, Oil of 48
Calciferol 20
Calciferol, Solution of 42
Calcium Acid Phosphate *75*
Calcium Chloride 21
Calcium Chloride, Hydrated 21
Calcium Gluconate 23
Calcium Hydroxide 24
Calcium Lactate *75*
Calumba 24
Canadian Committee on Pharmaceutical Standards, Introduction xix
Carbon Dioxide 24
Carbonate—
Bismuth 17
Potassium 55
Quinine Ethyl 58
Carvone in Oil of Caraway, and in Oil of Dill, Determination of *83*
Caseinate—
Sodium *78*

PAGE
Chenopodium, Oil of 49
Chiniofon. 25
Chlorides—
Calcium 21
Calcium, Hydrated 21
Ferric, Solution of 43
Ferrous, Citrated 33
Sodium, Injection of, and Acacia 39
Sodium, Physiological Solution of 45
Cinchophen 27
Citrated Ferrous Chloride 33
Citrates—
Iron *77*
Iron and Ammonium 33
Potassium 56
Sodium 62
Clinical Committee, Introduction xi
Cod-liver Oil 51
Colour Glasses for the Sulphuric Acid Test on Liquid Paraffin *84*
Committee of Civil Research, Sub-Committee on the British Pharmacopœia, Preface vii
Committee in India on Pharmacopœia Revision, Introduction xix
Corrigenda xxi
Cottonseed Oil *75*
Cresol with Soap, Solution of 43
Curd Soap 59
Cyclohexane *75*

Deletion xiv
Determination of Carvone in Oil of Caraway, and in Oil of Dill *83*
Determination of Esters in Volatile Oils *83*
Determination of Freezing-point, of Melting-point, and of Solidifying-point *79*
Determination of Optical Rotation *79*
Determination of Ultra-violet Absorption *81*
Determination of Viscosity *79*
2 : 6-Dichlorophenolindophenol *75*
2 : 6-Dichlorophenolindophenol, Solution of *75*
Digitalis, Fresh Infusion of 37
Digitalis, Powdered 27
Digitalis, Tincture of 67
Digitonin *76*
Dimethylaminobenzaldehyde, Solution of *76*
3 : 5-Dinitrobenzoyl chloride *76*
Diphenylbenzidine *76*
Diphtheria Prophylactic 68
Dry Extract of Stramonium 32

Editorial Committee, Introduction xiii

PAGE
Eosin 76
Eosin, Solution of 76
Epinephrine Hydrochloride Solution, *see* Liquor Adrenalinæ Hydrochloridi 42
Ergometrine 28
Ergot 29
Ergot, Liquid Extract of 29
Ergotoxine Ethanesulphonate 29
Errors of Biological Assays, General Notices 1
Esters in Volatile Oils, Determination of 83
Ethanesulphonate—
Ergotoxine 29
Ether 8
Extracts—
Extract of Belladonna, Liquid 29
Extract of Ergot, Liquid 29
Extract of Hyoscyamus, Liquid 30
Extract of Senega, Liquid 31
Extract of Stramonium, Dry 32
Extract of Stramonium, Liquid 31
Extract, Pituitary (Posterior Lobe) 30

Ferric Ammonium Sulphate and Hæmatoxylin, Solution of 77
Ferric Chloride, Solution of 43
Ferrous Chloride, Citrated 33
Formic Acid 76
Freezing-point, Determination of 79
Fresh Infusion—
Fresh Infusion of Digitalis 37
Fuller's Earth 76

Gas-gangrene Antitoxin (œdematiens) 9
Gas-gangrene Antitoxin (œdematiens), Biological Assay of . 102
Gas-gangrene Antitoxin (perfringens), Biological Assay of . 86
Gas-gangrene Antitoxin (vibrion septique) 12
Gas-gangrene Antitoxin (vibrion septique), Biological Assay of 106
General Chemistry Committee, Introduction xii
General Council of Medical Education and Registration of the United Kingdom vi
General Notices—
Errors of Biological Assays 1
Glass, Tests for Limit of Alkalinity of 117
Gluconate—
Calcium 23

Hæmatoxylin 76
Hæmatoxylin and Alum, Solution of 76
Hæmatoxylin and Ferric Ammonium Sulphate, Solution of . 77
Hard Soap 59
Histamine Acid Phosphate 35
Histaminæ Phosphas, *see* Histaminæ Phosphas Acidus . 35

PAGE
Hydrated Calcium Chloride 21
Hydrochloride—
Adrenaline, Solution of 42
Hydroxides—
Barium, Solution of, N/10 . . . . . *78*
Calcium 24
Potassium 56
Sodium 62
Hyoscyamus 36
Hyoscyamus, Liquid Extract of 30

Indicators employed in Volumetric Determinations and in *p*H Determinations *79*
Indigo Carmine 37
Infusion—
Infusion of Digitalis, Fresh 37
Injections—
Injection of Bismuth 37
Injection of Bismuth Oxychloride 38
Injection of Bismuth Salicylate 38
Injection of Mersalyl 39
Injection of Sodium Chloride and Acacia . . . 39
Injections, Methods of Sterilising Solutions for . . . *117*
Insulin 40
Introduction xi
Iodide—
Sodium *78*
Iodine, Aqueous Solution of 44
Iodine, Simple Solution of 45
Iodised Oil 49
Iodoform 41
Ipecacuanha 41
Ipecacuanha, Tincture of 67
Iron 34
Iron Citrate *77*
Iron and Ammonium Citrate 33
Irradiated Ergosterol, Solution of 43

Lactate—
Calcium *75*
Lactose 41
Lard 7
Lavender, Oil of 50
Lead, Quantitative Test for *82*
Lead Acetate 55
Lemon, Oil of 50
Limit of Alkalinity of Glass, Tests for *118*
Limits of error (Biological Assays)—
Antineuritic Vitamin (Vitamin B_1) *93*

Limits of error (Biological Assays) (*continued*)— PAGE
Antipneumococcus Serum (Type I)—
By the method of intraperitoneal injection into mice of mixtures of the serum being tested and the test dose of the culture *100*
By the method of intravenous injection into mice of the serum being tested, followed by the intraperitoneal injection of the test dose of the culture *101*
Antiscorbutic Vitamin (Vitamin C)—
Changes in the histological structure of the teeth. *95*
Growth, and development of macroscopic lesions of scurvy *96*
Gas-gangrene Antitoxin (œdematiens)—
By intramuscular injection into mice . . . *106*
By intracutaneous injection into guinea-pigs . . *106*
Gas-gangrene Antitoxin (vibrion septique)—
By intravenous injection into mice . . . *110*
By intracutaneous injection into guinea-pigs . . *110*
Staphylococcus Antitoxin—
By the haemolysis of washed red blood corpuscles of the rabbit *115*
By intracutaneous injection into guinea-pigs . . *116*
By intracutaneous injection into rabbits . . *116*
By intravenous injection into mice . . . *117*
By intraperitoneal injection into mice . . . *117*
Liniment of Belladonna 42
Liquefied Phenol 55
Liquid Extracts—
Liquid Extract of Belladonna 29
Liquid Extract of Ergot 29
Liquid Extract of Hyoscyamus 30
Liquid Extract of Senega 31
Liquid Extract of Stramonium 31
Liquid Paraffin 54
Liquid Paraffin, Colour Glasses for the Sulphuric Acid Test on *84*
Liquor Iodi Compositus, *see* Liquor Iodi Aquosus . . 44
Lugol's Solution, *see* Liquor Iodi Aquosus . . . 44

Magenta, Acid *77*
Marble *77*
Materials and Solutions employed in Tests . . . *75*
Melting-point, Determination of *79*
Menthol 46
Mercuric Oxycyanide 36
Mercury with Chalk 36
Mersalyl 46
Mersalyl, Injection of 39
Method, Suggested Details of (Biological Assays of):—
Vitamin A *87*
Antineuritic Vitamin (Vitamin B_1) *91*
Antiscorbutic Vitamin (Vitamin C) *94*
Antipneumococcus Serum (Type I) *98*

PAGE

Method, Suggested Details of (Biological Assays of) (*continued*)—
Antipneumococcus Serum (Type II) *102*
Gas-gangrene Antitoxin (œdematiens) *103*
Gas-gangrene Antitoxin (vibrion septique) . . . *107*
Staphylococcus Antitoxin *112*
Methods of Sterilising Solutions for Injection . . . *117*
Methyl Salicylate 48

β-Naphthol, Solution of 77
Neoarsphenamine 48
Normal Saline Solution, *see* Liquor Sodii Chloridi Physiologicus 45
Notice vi
Nutmeg, Oil of 52

Oil, Iodised 49
Oils, Determinations and Tests—
Oil of Caraway, Determination of Carvone in . . *83*
Oil of Dill, Determination of Carvone in . . . *83*
Oils, Essential—
Oil of Cajuput 48
Oil of Chenopodium 49
Oil of Lavender 50
Oil of Lemon 50
Oil of Nutmeg 52
Oil of Peppermint 51
Oil of Siberian Fir 48
Oil of Rosemary 53
Oil of Sandal Wood 53
Oil of Turpentine 53
Oils, Fixed—
Oil, Arachis *75*
Oil, Cod-liver 51
Oil, Cottonseed *75*
Oil, Olive 52
Ointments—
Ointment, Simple 71
Ointment of Sulphur 71
Olive Oil 52
Optical Rotation, Determination of *79*
Oxycyanide—
Mercuric 36
Oxychloride—
Bismuth 18
Bismuth, Injection of 38
Oxygen 54

Papers published in scientific periodicals, Introduction . xvi
Paraffin, Liquid 54
Peppermint, Oil of 51
Pharmaceutical Chemistry Committee, Introduction . . xiii

PAGE
Pharmacology Committee, Introduction . . . xii
Pharmacy and Pharmacognosy Committee, Introduction . xii
*p*H Determinations and Volumetric Determinations, Indicators employed in *79*
Phenol, Liquefied 55
Phenolphthalein 55
Phenylhydrazine *77*
Phosphates—
Calcium Acid *75*
Histamine Acid 35
Potassium *77*
Sodium 63
Physiological Saline Solution, *see* Liquor Sodii Chloridi Physiologicus 45
Physiological Solution of Sodium Chloride 45
Picrolonic Acid *77*
Pituitary (Posterior Lobe) Extract 30
Potassium Bicarbonate 55
Potassium Carbonate 55
Potassium Citrate 56
Potassium Hydroxide 56
Potassium Phosphate *77*
Powdered Digitalis 27
Powdered Digitalis, Biological Assay of *86*
Precipitated Bismuth 19
Preface vii
Pulvis Chiniofoni, *see* Chiniofonum 25
Pyridine *77*
Pyroxylin 58

Qualitative Reactions and Tests for Substances mentioned in the Pharmacopœia *82*
Quantitative Test for Arsenic *82*
Quantitative Test for Lead *82*
Quinine Bisulphate *77*
Quinine Ethyl Carbonate 58

Reports of Committees, Introduction xv
Rhubarb 58
Rice Starch *77*
Rosemary, Oil of 53

Salicylates—
Bismuth, Injection of 37
Methyl 48
Sandal Wood, Oil of 53
Senega, Liquid Extract of 31
Serum, Antipneumococcus (Type I) 60
Serum, Antipneumococcus (Type I), Biological Assay of . *97*
Serum, Antipneumococcus (Type II) 61
Serum, Antipneumococcus (Type II), Biological Assay of . *102*
Siberian Fir, Oil of 48

PAGE
Silver Protein 15
Silver Proteinate, *see* Argentoproteinum 15
Simple Ointment 71
Simple Solution of Iodine 45
Soap, Curd 59
Soap, Hard 59
Soap, Soft 59
Sodium Bismuthyltartrate 17
Sodium Caseinate *78*
Sodium Chloride, Physiological Solution of . . . 45
Sodium Chloride and Acacia, Injection of 39
Sodium Citrate 62
Sodium Hydroxide 62
Sodium Iodide *78*
Sodium Phosphate 63
Sodium Thiosulphate 63
Soft Soap 59
Solidifying-point, Determination of *79*
Solutions—
Solution, Epinephrine Hydrochloride, *see* Liquor Adrenalinæ Hydrochloridi 42
Solution of Adrenaline Hydrochloride 42
Solution of Barium Hydroxide, N/10 . . . . *78*
Solution of Calciferol 42
Solution of Cresol with Soap 43
Solution of 2 : 6-Dichlorophenolindophenol . . . *75*
Solution of Dimethylaminobenzaldehyde . . . *76*
Solution of Eosin *76*
Solution of Ferric Chloride 43
Solution of Hæmatoxylin and Alum *76*
Solution of Hæmatoxylin and Ferric Ammonium Sulphate *77*
Solution of Iodine, Aqueous 44
Solution of Iodine, Simple 45
Solution of Irradiated Ergosterol 43
Solution of β-Naphthol *77*
Solution of Sodium Chloride, Physiological . . . 45
Solution of Trinitrophenol and Acid Magenta . . *78*
Solutions employed in Volumetric Determinations . *78*
Solutions for Injection, Methods of Sterilising . . *117*
Solutions and Materials employed in Tests . . . *75*
Squill, Vinegar of *4*
Standard Preparations—
Vitamin A *86*
Antineuritic Vitamin (Vitamin B_1) *91*
Antiscorbutic Vitamin (Vitamin C) *93*
Antipneumococcus Serum (Type I) *97*
Antipneumococcus Serum (Type II) *102*
Gas-gangrene Antitoxin (œdematiens) *102*
Gas-gangrene Antitoxin (vibrion septique) . . . *107*
Staphylococcus Antitoxin *111*
Staphylococcus Antitoxin 11
Staphylococcus Antitoxin, Biological Assay of . . . *111*

PAGE

Starch 9
Starch, Rice 77
Sterilised Water 14
Stramonium, Dry Extract of 32
Stramonium, Liquid Extract of 31
Stramonium, Tincture of 67
Strong Protein Silver, *see* Argentoproteinum . . . 15
Sulphanilic Acid 78
Sulpharsphenamine 64
Sulphates—
Atropine 16
Zinc 72
Sulphur Dioxide 78
Sulphuric Acid (50 per cent. v/v) 78
Sulphuric Acid Test on Liquid Paraffin, Colour Glasses for . 84
Sulphur, Ointment of 71

Tartrate—
Bismuth Sodium, *see* Bismuthi et Sodii Tartras . . 17
Tests and Qualitative Reactions for Substances mentioned in the Pharmacopœia 82
Tests for Limit of Alkalinity of Glass . . . 118
Theophylline 64
Thiosulphate—
Sodium 63
Thiosulphates, Qualitative Reactions and Tests for . . 82
Thyroxine-sodium 66
Thyroid 65
Tinctures—
Tincture of Digitalis 67
Tincture of Ipecacuanha 67
Tincture of Stramonium 67
Trinitrophenol and Acid Magenta, Solution of . . . 78
Tryparsamide 69
Turpentine, Oil of 53

Union of South Africa, Department of Public Health, Introduction xix
Units—
Vitamin A 87
Antineuritic Activity (Vitamin B_1) 91
Antiscorbutic Activity (Vitamin C) 94
Antipneumococcus Serum (Type I) 97
Antipneumococcus Serum (Type II) 102
Gas-gangrene Antitoxin (œdematiens) 103
Gas-gangrene Antitoxin (vibrion septique) . . . 107
Staphylococcus Antitoxin 111
Ultra-violet Absorption, Determination of 81

Valerian 71
Vinegar of Squill 4
Viscosity, Determination of 79

PAGE

Vitamin Committee, Introduction xiii

Vitamins—

Vitamin A, Assay of *86*
Standard Preparation *86*
Unit *87*
Suggested Details of Biological Method . . *87*
Suggested Details of Spectrophotometric Method . *89*
Vitamin B_1, Adsorbate of *57*
Vitamin C, *see* Acidum Ascorbicum 4

Vitamins, Biological Assays—

Vitamin B_1, Biological Assay of Antineuritic Vitamin . *91*
Standard Preparation *91*
Unit *91*
Suggested Details of Method *91*
Vitamin C, Biological Assay of Antiscorbutic Vitamin . *93*
Standard Preparation *93*
Unit *94*
Suggested Details of Method *94*
Vitamin D, Biological Assay of Antirachitic Vitamin . *84*
Volatile Oils, Determination of Esters in *83*
Volumetric Determinations, Solutions employed in . . *78*
Volumetric Determinations and *p*H Determinations, Indicators employed in *79*

Water, Sterilised 14
Weights and Measures *118*
Wool Fat 7

Yellow Beeswax 25

Zinc Sulphate 72

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